Arizona Medicine

JOURNAL OF ARIZONA MEDICAL ASSOCIATION

MEDICAL SOCIETY OF THE UNITED STATES AND MEXICO

Volume 18 Number 1

January, 1961

resistant
staphylococci
among
outpatients
emerge
less
frequently...
disappear
more
readily

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chloramphenicol, Parke-Davis

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Goslings and Büchli[2] report that "...resistance was lost entirely after 3 months..." in the small percentage of patients who carried staphylococcal strains resistant to CHLOROMYCETIN. Numerous other investigators concur in the observation that staphylococcal resistance to CHLOROMYCETIN is of a low order.[3-8]

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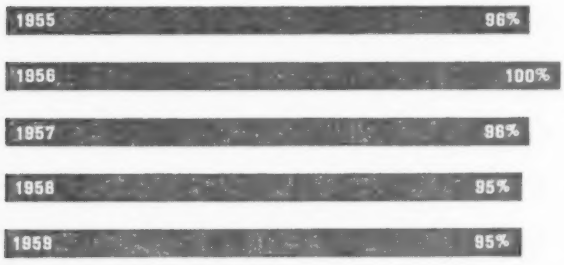
References: (1) Bauer, A. W.; Perry, D. M., & Kirby, W. M. M.: *J.A.M.A.* **173**:475, 1960. (2) Goslings, W. R. O., & Büchli, K.: *Arch. Int. Med.* **102**:691, 1958. (3) Goodier, T. E. W., & Parry, W. R.: *Lancet* **1**:356, 1959. (4) Fisher, M. W.: *Arch. Int. Med.* **105**:413, 1960. (5) Petersdorf, R. G., *et al.*: *Arch. Int. Med.* **105**:398, 1960. (6) Glas, W. W., in Symposium on Antibacterial Therapy, Michigan & Wayne County Acad. Gen. Pract., Detroit, September 12, 1959, p. 7. (7) Modarress, Y.; Ryan, R. J., & Francis, Sr. C. E: *J. M. Soc. New Jersey* **57**:168, 1960. (8) Rebhan, A. W., & Edwards, H. E.: *Canad. M. A. J.* **82**:513, 1960.

IN VITRO SENSITIVITY OF COAGULASE-POSITIVE STAPHYLOCOCCI TO CHLOROMYCETIN FROM 1955 TO 1959*



These sensitivity tests were done by the disc method on 310 strains of coagulase-positive staphylococci. Strains were isolated from patients seen in the emergency room. It should be noted that among inpatients, resistant strains were considerably more prevalent.

*Adapted from Bauer, Perry, & Kirby[1]

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Arizona Medicine

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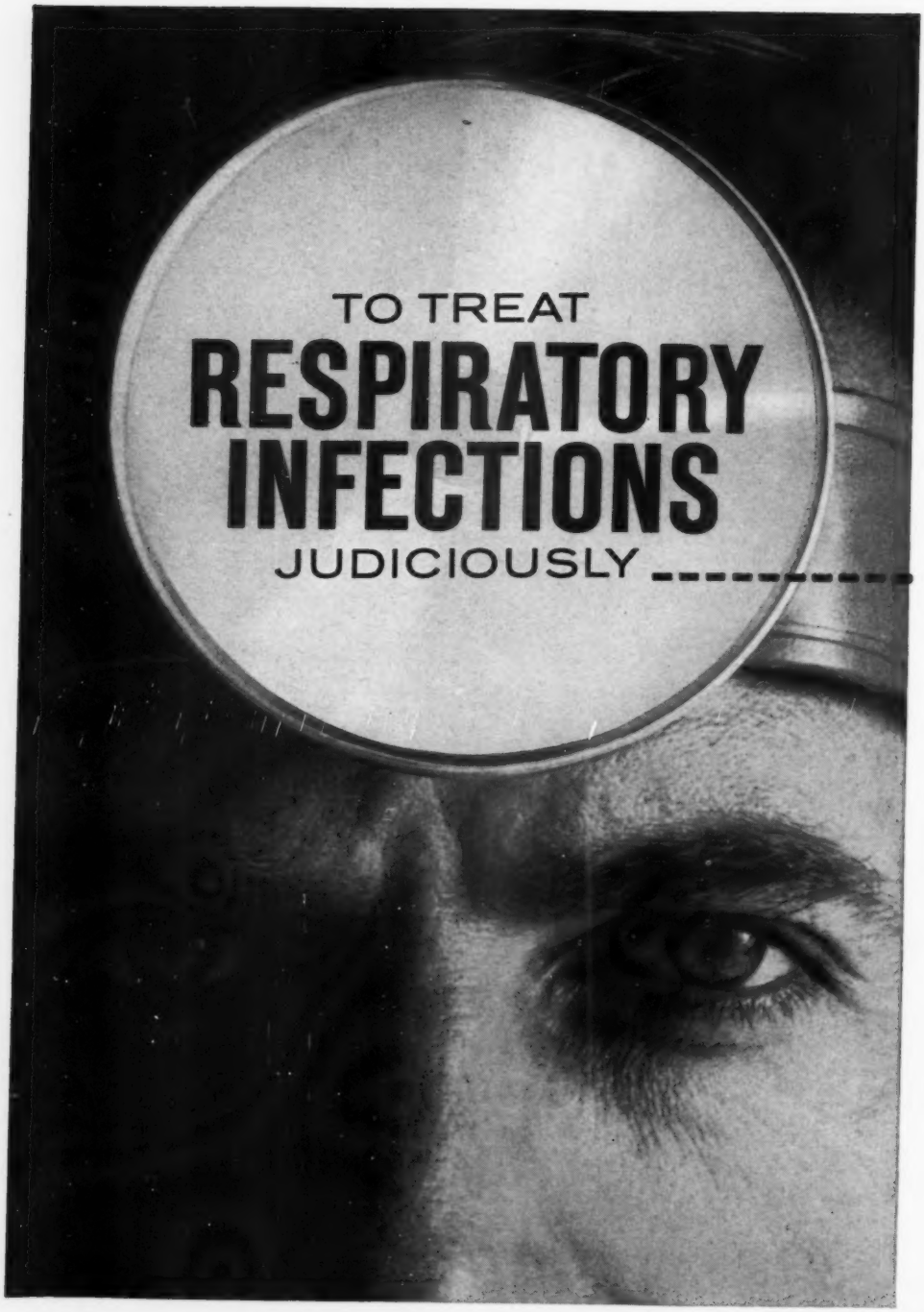
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Arizona Medical Association Reports

Arizona Medicine

Vol. 18, No. 1 January, 1961

Board of Directors

Meeting of the Board of Directors of The Arizona Medical Association, Inc., held Sunday, October 23, 1960, Scottsdale, Arizona, convened at 10:15 A.M., Clarence E. Yount, Jr., M.D. (Vice-President), Chairman, presiding.

ROLL CALL

Present: Drs. Beaton, Lindsay E., President; Dudley, Jr., Arthur V., Dysterheft, Arnold H., Hamer, Jesse D., Hileman, Walter T., Jarrett, Paul B., Melick, Dermont W., Polson, Donald A., Reed, Wallace A., Running, E. Henry, Smith, Leslie B., President-elect; Steen, William B.; Tuveson, Leo L.; Yount, Jr., Clarence E., (Vice-President), Chairman.

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BENEVOLENT AND LOAN FUND

Messers. Duncan Newell and John McCarthy, representing the Trust Department of The Valley National Bank, were present, together with Mr. Edward Jacobson, Counsel of this Association, to present a proposed Trust Agreement suggested in the handling for the Association, its Student Loan activity now being conducted by and as a part of the Benevolent and Loan Fund Committee operation. Mr. Jacobson reviewed the contents and explained the provisions contained in the (a) "Declaration of Trust Creating and Governing the Arizona Medical Association Benevolent and Loan Fund Trust", (b) "Loan Agreement," (c) "Form of Certification by the Association's Benevolent and Loan Fund Committee of Student Loan Granted," and (d) "Form of Request for Change in Terms." Considerable discussion ensued and the representatives present were subjected to detailed questioning.

Regarding the cost of operation, Mr. Newell stated that the annual rate is $6.00 per $1,000.00 market value incurred with the Trust Agreement; i.e. if the market value is established at $50,000.00, the annual fee would be $300.00; if $15,000.00, the fee would be $90.00, etc., with a minimum charge of $100.00, exclusive of unusual expense which may develop in the process of collection of loans which, of course, would be an additional charge.

It was moved by Doctor Reed, seconded by Doctor Jarrett and others and unanimously carried that the Board accept the proposed trust of its Benevolent and Loan funds through The Valley National Bank for a trial period of one year and authorize execution of the necessary Trust Agreement(s).

CHAPTER 13 MEDICINE & SURGERY, A.R.S. 1956

Counsel reviewed in detail his report on prog-

ress made to date in the study of possible amendments to Chapter 13 Medicine and Surgery (Act), A.R.S. 1956, which already has consumed considerable time. It was his opinion that to rewrite the entire Act will require considerably more time and research and is not possible of achievement in time for presentation during the forthcoming Legislative Session, taking into account his time-table. Question was raised as to whether there are some few emergency amendments desirable at this time which could rather simply be prepared for action in the Legislature this coming year.

Considerable discussion ensued. It was the general concensus that a piecemeal approach is not desirable and should be avoided if at all possible. On direct questioning, the Executive Secretary stated that at no time had he considered the need less than a complete rewrite of the entire statute. To do less would not be accomplishing the necessary and essential objective; recognizing, however, that the Board of Medical Examiners had expressed a desire to achieve certain immediate relief in portions giving it most concern, it was his opinion that the next step would be to have a joint meeting between members of the State Board and the Association to review the entire problem and establish a workable time schedule to achieve the objective. Many matters of medical policy must be determined and decisions arrived at before proceeding with the mechanics of preparing specific amendments.

It was moved by Doctor Reed, seconded by Doctor Steen and unanimously carried that the President be authorized to appoint a committee of this Association to meet with the Board of Medical Examiners for the purpose of giving further study to this matter, the committee to be given authority to determine whether or not preparation of amendments piecemeal are indicated and desirable at this time.

The President appointed: Doctors Jesse D. Hamer (Phoenix) to serve as chairman; Paul B. Jarrett (Phoenix), Wallace A. Reed (Phoenix) and William B. Steen (Tucson) to serve as members of this committee, with the President, Doctor Lindsay E. Beaton (Tucson) and President-elect Doctor Leslie B. Smith (Phoenix) likewise to serve as members ex-officio. A joint meeting with the Board of Medical Examiners is to be called at the earliest possible time.

ACTING SECRETARY

Due to the continuing illness of the Secretary, Lorel A. Stapley, M.D., the President recommended the appointment of the President-elect, Leslie B. Smith, M.D. to serve ac Acting Secretary until such time as Doctor Stapley is able to resume his duties. Doctor Smith indicated willingness to accept such appointment.

It was moved by Doctor Beaton, seconded by Doctor Steen and unanimously carried that Doctor Leslie B. Smith, President-elect, be appointed Acting Secretary of this Association to serve until such time as Doctor Stapley is able and willing to resume his duties as Secretary (or until his term expires).

EXECUTIVE COMMITTEE MEETINGS REPORTS

Meetings of June 26 and September 18, 1960

Lindsay E. Beaton, M.D., President and Chairman of the Executive Committee, reported on matters coming before that Committee in meetings held June 26 and September 28, 1960, covering the following matters, a detailed report having been prepared and circulated among the members of this Board and authorized filed with the proceedings of this meeting:

Referred to the Medical Economics Committee for study and report:

(a) AMA-sponsored group annuity and disability program; (b) California-Western States Insurance Company group insurance plan; (c) American Academy of General Practice retirement program; (d) Simpson-Keogh Bill, with instruction to study ways of implementing such legislation in the practical interest of the doctor, should it ever be passed, and to study the "Kintner Plan"; and (e) ARMA House of Delegates' resolution adopted in 1960 referable to the establishment of a program of voluntary health and accident insurance for older citizens, with special regard to the development of non-cancellable health insurance policies.

Referred to the Professional Committee for study and report:

(a) AMA Conference on Pregnancy and Perinatal Morbidity; (b) ARMA House of Delegates' resolution adopted in 1960 offering help in the establishment of adult mental health clinics; (c) the matter of payments to Comstock Hospital in Tucson, where it is more practical to care for children with chronic diseases, by

Blue Cross-Blue Shield Plans; and (d) to seek information from other states as to how much help a Cancer Registry is, what safeguards against name revealing are afforded, so that this information may be used in influencing legislators previously opposed to the idea of a Cancer Registry, in order that the Association may determine the practability of pushing cancer legislation registration again this coming year.

The Executive Committee determined to schedule a meeting with members of the Ministerial Association and the Arizona State Nurses Association to discuss problems of mutual interest.

Referred to the Professional Liaison Committee for study and report:

(a) AMA program materials on careers in medicine for high school students with instruction to initiate the careers program as soon as possible in both high schools and colleges; (b) Resolution of Maryland Society regarding cutting off care of all non-service-connected cases in VA hospitals, with special request that Dean's Committee of VA be contacted to see what the implementation of such a request might do to teaching in the country's medical schools; (c) AMA House of Delegates' resolution on the National Foundation; and (d) AMA House of Delegates' resolution referable to recruitment of medical representatives of the Arizona Education Association, with further instruction to the subcommittee on Careers to develop plans for "Career Nights" at both ASU and U. of A.

President directed to write an official letter seeking clarification of stand on the resolution made by the Governor's Conference in Montana and asking what plans will be made for implementation of the matching funds requirement of the Mills Bill.

Referred to the Articles of Incorpration and By-Laws Committee for study and report:

(a) The matter of consideration of need for the preparation of a by-laws change to provide for the appointment of acting officers in case of prolonged absence of regular officers as recently experienced in the office of Secretary.

Referred to the Public Relations Committee:

For implementation: (a) ARMA House of Delegates' resolution adopted in 1960 with instruction to devise a proper public educational program on federalized medical plans, prepare budget, and clear its final program with the Executive Committee; (b) AMA House of Delegates' resolution recommending that physicians be more active in public affairs; (c) AMA House of Delegates' resolution re recruitment of medical students; (d) report of Chairman of subcommittee on Aging of the Professional Committee, for guidance, with the caution that the report of Emory University sociologists being so heavily stressed by AMA, be carefully considered in the light of adverse reactions reported in the September 2 issue of "Science," AMA to be contacted for possible rebuttal to the "Science" stand; and (e) directing maximum publicity in the program of student loans under the Benevolent and Loan Fund Committee.

Referred to the Legislative Committee for study and report:

The matter of Cancer Registry to explore the practicability of introducing for enactment by the 25th Legislature of Arizona a measure providing for a State-wide Cancer Registry.

Referred to the Benevolent and Loan Fund Committee for development:

A plan that will ensure an on-going program through procurement of contributions from doctors and non-medical sources, the fund currently nearing exhaustion.

Referred to the Scientific Assembly Committee:

(a) Instruction to begin planning for the Diamond Jubilee of the Association; and (b) to consider scheduling of annual meetings two or three years in advance to reserve dates and adequate places.

Referred to the Industrial Relations Committee for study and report:

Complaints in the matter of Industrial Commission interference with physician care of ICA clients, and in addition, the President and Counsel are to seek an audience with the Industrial Commissioners.

Matters disposed of, recorded for reference:

1. Authorized telegrams to U. S. Representatives and Senators regarding Association stand against Forand-type legislation, in favor of the Mills Bill, except for the section approving inclusion of doctors under Social Security;

2. Approved poison control information file cards be made available to osteopathic hospitals;

3. Determined Diabetes Detection Drives should remain with component societies;

4. Noted that the state law, if enforced, will allow the picking-up and detention of men discharged, although still active, from VA hospitals for disciplinary reasons;

5. Endorsed the stand of Arizona State Board of Pharmacy that no prescription more than one year old be refilled;

6. Instructed President not to accept invitation to October Osteopathic National Meeting scheduled for Phoenix;

7. Agreed not to approve any official Asssociation support of any candidates for any office in the November national election;

8. Approved invitation to Board meetings of major committee chairmen to discuss matters on which special information required;

9. Approved attempt to gain audience with Government following the election in an endeavor to obtain better representation of Medical Association opinion in the appointment of physicians to commissions, etc. having to do with public health;

10. Approved meeting with President of Women's Auxiliary;

11. Approved organizational chart and framing, to be hung in the Central office; and

12. Approved Accounting procedures: (a) Marvin Henry, CPA, Phoenix, hired as accountant; (b) agreed to preparation of monthly financial statements by Central Office; (c) determined books to be kept and maintained in Central Office; (d) approved two-signature system for voucher check payments; (e) authorized accounts of Association be split so as to take full advantage of federal insurance; (f) authorized Association funds be placed in Phoenix (Park Central Branch of Valley National Bank) for convenience of auditor and Central Office; (g) Treasurer henceforth to act as financial officer and advisor of the Association, no longer required to be its bookkeeper; and (h) approved purchase of APECO copying equipment.

Memberships

Determined county societies shall make decision regarding transfer of 70-year members no longer in active practice to Associate membership to assure accuracy in roster of Active members in computing membership to AMA, Central Ofifce to make query of this group annually to determine Active or Inactive status.

Approved attendance of President, President-elect, AMA Delegate and Executive Secretary to Salt Lake City Conference July 29 and 30, 1960, at Association expense.

Instructed Counsel and Executive Secretary to analyze possibility of rewriting the Medical Practice Act.

Authorized execution of Medicare supplemental agreements of (a) negotiated claim rate, (b) limitation on invoicing, and (c) modification of portions of Medicare Manual and Schedule Allowances on recommendation of Fiscal Administrator.

Approved action of Editor-in-Chief, President and Executive Secretary, on advice of Counsel, in disposing of all claims of the former publisher of Arizona Medicine, J. N. McMeekin, for a sum of $480.50.

Authorized additional 1960 annual meeting expenditure payments of (a) $70.00 to Arizona Pediatric Society to cover luncheon expenses not met by guests; (b) $30.00 to Golf Chairman for unexpected expenses; and (c) $30.00 to Safari Hotel for coffee consumed during "coffee hour" — reimbursed by Arizona Drug Travellers in August, 1960.

Resolved that only such attendance as deemed essential to meetings scheduled by AMA et al., will be approved at Association expense; however, effort to be made to find a representative who may be in attendance for personal reasons and can simultaneously act as the Association's envoy.

Noted reduction in printing costs of Arizona Medicine by about $2,000 per year, the result of economies effected.

It was moved by Doctor Beaton, seconded by Doctor Running and unanimously carried that the report covering the meetings of June 26 and September 18, 1960 of the Executive Committee of the Board of Directors be accepted.

Meeting of October 22, 1960

Doctor Beaton reported the results of the meeting held yesterday, October 22, 1960, included the following items:

A meeting was held with the Arizona Ministerial Association in the matter of repeal of that portion of Title 25, Marital and Domestic Act, Chapter I, Section 25-103.01 through 103-10 A.R.S. 1957, dealing with examination and certification requiring a standard serological test. It was unanimously agreed at the end of this meeting that it would be impractical to try to change the law now because any change would be unacceptable to the public, but that, rather, we would appoint two ad hoc committees which would get together in a joint effort in public relations to point out the facts about

serological tests; point out to the public that a false positive may occur and that therefore all persons in Arizona intending to get married should have an examination by their physician 30 days ahead of time. The ministers felt that this was a proper thing to do and they thought that it would further save the pathologists from any allegation that they are sponsoring a questionable test procedure just to make money. We are going to ask the members of the Jewry and members of the Catholic priesthood to such a meeting. This proved to be a very helpful meeting because everybody ended up with good feelings about it and we felt that it was a useful solution to the problem that was raised by the Professional Committee's motion of last year; so the Executive Committee was therefore advised that such an ad hoc committee be appointed.

It was moved by Doctor Jarrett, seconded by Doctor Steen and unanimously carried that the membership of the ad hoc committee representing this Association to meet with a similar committee of the Ministerial Association comprising Derrill B. Manley, M.D., (Phoenix) Chairman; Philip G. Derickson, M.D. (Tucson), James D. Barger, M.D. (Phoenix), Leo L. Tuveson, M.D. (Phoenix) — recommended appointed by the President, be approved.

Meeting with representatives of the Arizona State Nurses Association, Inc. in discussion of matters of mutual interest, resulted in agreement that our Executive Secretaries would try to maintain better liaison; that liaison would be expected between specific committees of the Nurses Association and ours, such as the Legislative Committee, and so on; and that our Professional Liaison Committee would continue to be active in its subcommittee on Nursing, and that they (the Nurses) would appoint an ad hoc committee of their own to consult with it when there arose any cause for exploration of a problem.

Effective October 1, 1960 the Active (Voting) membership of ARMA totalled 981, resulting in an allocation of 67 Delegates and Alternates to its House of Delegates, two each for each component county medical society, with the exception of Maricopa, with an Active Membership of 553, resulting in allocation of 29 Delegates and Alternates, and Pima, with an Active membership of 262, resulting in the allocation of 14 Delegates and Alternates, in accordance with the by-laws. As to the composite of the Board of Directors, such total Active voting membership will provide for the allocation of 22 resulting in an increase of one, for a total of six Central District Directors comprising Maricopa Society, and an increase of one for a total of three Southern Directors, comprising Pima Society.

The Treasurer's report of the financial status of this Association on a semi-annual fiscal basis to September 30, 1960, prepared by the appointed accountant (without certified audit), reviewed. Again, it was determined that monthly financial statements will be provided the Executive Committee, a semi-annual auditor's report supplied the Board of Directors, and a certified annual audit provided both the Board of Directors and House of Delegates at the close of the fiscal year. Auditor's recommendations: (a) consider use of complete budget for ensuing year, including both revenues and expenditures; (b) consider application of an amount based upon a practical cost computation to be borne by the Publishing Committee each month representing an additional cost for publication of the Journal, thereby reflecting a true cost; and (c) assignment to one particular savings account, interest earned to date representing the "benevolence" portion of the Benevolent and Loan Fund operation.

It was moved by Doctor Hileman, seconded by Doctor Dysterheft and unanimously carried that the recommendations of the auditor be approved.

It was further requested that study be given the desirability of continuing the accounting operations of this Association on a fiscal year basis versus a calendar year basis.

Approved establishment of the following monthly operational costs associated with the Journal: (a) salaries, $200.00; (b) telephone, $26.20; (c) rental of office space, $100.00; (d) miscellaneous supplies, $10.00; and (e) equipment depreciation, $7.00.

Agreed to the establishment of a "deferred income" account or "reserve" for anticipated expenditures resulting in a true picture of accounting associate with annual meeting operations.

Approved payment of $9,697.50 to AMEF representing allocated portion of dues collections for the period ending September 30, 1960; and establishing hereafter the latter date (September 30) as the annual date for computing such contributions.

Authorized attendance of AMA Delegate and Executive Secretary to special meeting called by AMA to be held in Washington, D. C. November 27, 1960, just prior to the opening of the Clinical Session, for the purpose of bringing state medical association representatives to date on national developments pertaining to health care of the indigent and medical indigent aged (those over 65 years of age).

Approved objectives of establishment of a joint council to improve the health care of the aged sponsored by ADA, AHA, and AMA and the American Nursing Home Association, referring the matter to the subcommittee on Aging of the Professional Committee for implementation. Communications from the Arizona Dental Association and the Arizona Association of Nursing Homes were received, expressing their willingness to cooperate in furtherance of this effort.

Recommended appointments by the State Chairman of the Governor's Committee on Aging for the White House Conference on Aging, of Jesse D. Hamer, M.D. of Phoenix and Clarence L. Robbins, M.D. of Tucson, as Delegates to be appointed by Governor Fannin to the White House Conference on Aging, January 9, 1961, in Washington, D. C., the Delegates to be responsible for part or all of their expenses. Referred to the Board of Directors without recommendation, however expressing satisfaction in the choice of the two Delegates mentioned.

Recommended calling a joint conference with the Arizona Pharmaceutical Association referable to dispensation of unlabelled drugs.

The AMEF award of merit and citation to Herbert D. Welsh, M.D., in recognition of his work on behalf of medical education, to be presented to the doctor at the next regular meeting of the Pima County Medical Society. It was suggested that such financial contributions, the outgrowth of the "Arizona Plan" (contributions from pharmacists, etc. to AMEF rather than donation of Christmas presents to physicians) might in the future be considered for contributions to the Association's own Benevolent and Loan Fund Committee, augmenting monies to be made available to assist worthy Arizona medical students in furthering a medical career.

Referred back to the Industrial Relations Committee for direct referral to Maricopa County Medical Society were charges in the case of V. Eugene Frazier, M.D. of Mesa, Howard C. Lawrence, M.D. of Phoenix, and Rexford A. Peterson, M.D. of Phoenix.

Denied reinstatement of the membership of Ruth Alice Johnson, M.D. (Maricopa Society) as an Associate member, account: current out-of-state residence and lack of by-laws provision to cover such situation.

Granted Active membership status, dues exempt, effective January 1, 1961, account: attaining the age of 70 years, for Nathan Schneck, M.D. and Dan L. Mahoney, M.D., both of Tucson (Pima Society).

Referred to Board of Directors without recommendation, Tucson Obstetrical and Gynecological Society resolution, with endorsement of Pima County Medical Society, referable to an amendment of Section 13-213, A.R.S., in the matter of giving of contraceptive advice, proposing deletion of the words: "or for prevention of conception." It was indicated that similar action had been taken by the Maricopa County Society Board of Directors.

It was moved by Doctor Jarrett, seconded by Doctor Reed and unanimously carried that such action be approved and the matter referred to the Legislative Committee with the recommendation that they devolve some plan of doing away with this piece of legislation.

Referred to Irving L. Folberg, M.D. of Sierra Vista, Arizona, report of the AMA Delegate pertaining to "osteopathy" in the matter of practice of M.D.s in an osteopathic hospital.

Referred to Professional Committee for investigation and report, operations of the North Western Clinical Laboratory of Phoenix offering clinical laboratory services to physicians and soliciting participation on a subscription basis.

Referred to the Public Relations Committeee for review and recommendation, the matter of selection of qualified participants among Association members, associate with the proposed "community service award for physicians" to be offered by A. H. Robins Company.

The subcommittee on Public Health and Schools of the Professional Liaison Committee reports no special need for legislation during the forthcoming Legislative Session in the matter of "raw milk"; suggested amendment to legislation pertaining to birth control, especially as pertains to making available information dealing with contraceptive advice; and minor changes to be promulgated by the State Department of Public Health amending the present health code.

No action taken regarding financial contribu-

tion to the 66th National Conference on Government, to be held in Phoenix November 13-16, 1960.

Referred to the Industrial Relations Committee for investigation and report, the matter dealing with reporting and establishing of the per cent loss of vision sustained by industrial patients, especially when only one eye is involved.

It was moved by Doctor Beaton, seconded by Doctor Running and unanimously carried that the report covering the meeting of October 22, 1960 of the Executive Committee of the Board of Directors be accepted.

ATOMIC ENERGY COMMITTEE OF ARIZONA

Doctor Beaton reported that the Governor had appointed R. Lee Foster, M.D. of Phoenix, a member of his Atomic Energy Committee of Arizona.

EXECUTIVE COMMITTEE RECOMMENDATIONS REFERRED TO THE BOARD OF DIRECTORS

Central Office

It was moved by Doctor Polson, seconded by Doctor Dudley and unanimously carried that the President, President-elect, Vice-President, Secretary and Treasurer be designated alternate officers to be authorized to sign voucher checks of the Association in the instance of the unavailability, because of illness or otherwise, of the Treasurer and/or Secretary, to assure continuity of operations.

It was moved by Doctor Dudley, seconded by Doctor Tuveson and unanimously carried that the General Fund checking account of this Association be transferred from the Campbell-Grant Branch of the Valley National Bank, Tucson, to the Park Central Branch of the Valley National Bank in Phoenix.

It was moved by Doctor Polson, seconded by Doctor Hileman and unanimously carried that the following additional sums be appropriated for expenditure during the remaining fiscal year, associate with the budget of appropriations for the fiscal year 1960-61; telephone and telegraph, $600.00; supplies, $1,000.00; postage, $500.00; Board of Directors, $300.00; miscellaneous committees, $600.00; furniture and fixtures, $1300.00 (including authorized purchase of new APECO equipment and adjustment in typewriter equipment replacement).

Further consideration is to be given the need for an additional appropriation in the instance of the Public Relations Committee if, as and when a program is developed and approved by the Board of Directors.

Deferred action in the transfer from Active membership to Associate membership, account: retirement, dues exempt, in the instances of Henry Leroy Franklin, M.D. and Joseph Madison Greer, M.D. (Maricopa County Medical Society) to determine their individual wishes and possible effect upon their group insurance for accident and sickness should they be participants.

Professional Committee

Ratified mail vote of Board members, nineteen approving, one not voting (account illness), statement of position of this Association dealing with medical care of the aged in accord with the position of AMA expressed at its annual meeting June last, which is to be included in the report to the Governor being prepared by the Governor's Committee on Aging.

It was moved by Doctor Reed, seconded by Doctor Tuveson and unanimously carried that the expenses of the Delegates, Doctors Hamer and Robbins, to the White House Conference on Aging, to be held in Washington, D. C. January 9-13, 1961, be approved, provided that they are nominated by the Governor and finally approved by the Executive Committee of the Board of Directors.

It was moved by Doctor Tuveson, seconded by Doctor Reed and unanimously carried that the Arizona Division of the American Cancer Society be privileged to use the name of this Association as a cooperating agency associate with its Ninth Annual Cancer Seminar to be held in Tucson, Arizona, at the Tidelands Motor Inn, January 12 through 14, 1961.

It was moved by Doctor Hileman, seconded by Doctor Steen and unanimously carried that the matter of approval and concurrence in the Duval County (Florida) Medical Society's findings contained in its resolution adopted June 7, 1960, opposing certain recommendations of the Joint Commission on Accreditation of Hospitals, be tabled.

It was moved by Doctor Polson, seconded by Doctor Tuveson and unanimously carried that there be established a State-wide Maternal and Infant Mortality Committee to study each death within Arizona, the statistics to be promulgated by the Arizona State Department of Health,

analysis to be made through the subcommittee on Maternal and Child Health with the assistance of the State Pediatric and Obstetrics Societies.

It was moved by Doctor Dudley, seconded by Doctor Tuveson and unanimously carried that the subcommittee on Mental Health of the Professional Committee of the Association be directed to act in a consulting capacity to those professional and lay groups seeking advice in the selection of qualified experts as speakers and/or instructors in the field of hypnosis, when requested.

Professional Liaison Committee

It was moved by Doctor Singer, seconded by Doctor Hileman and unanimously carried that the resignation of Chester G. Bennett, M.D. (of Phoenix) as a member of the Professional Liaison Committee for the term 1960-63 be accepted; and that Albert G. Wagner, M.D. (of Phoenix), on recommendation of the President, be appointed a member of the Professional Liaison Committee to fill the unexpired term, he to be assigned the chairmanship of the subcommittee on Careers and Arizona AMEF.

It was moved by Doctor Beaton, seconded by Doctor Hileman and unanimously carried that the Arizona State Board of Health be informed that the subcommittee on Public Health and Schools of the Professional Liaison Committee stands ready and willing to volunteer its services for screening and interviewing candidates in the selection of a Commissioner of the Arizona State Department of Health.

Approved the form letter of inquiry to be circulated among the members of the Association, with questionnaire response card, seeking participants in the development of a school health consultant program, as approved for activation by the ARMA House of Delegates in May of 1960.

It was moved by Doctor Dysterheft, seconded by Doctor Running and unanimously carried that the matter of promulgation of a list of four names of members of this Association be submitted to the Governor as nominees from among which he will appoint one to serve as a member of the Advisory Survey and Construction Council for a term of four years, effective January first next, to fill the anticipated vacancy, which assignment is currently filled by William B. Steen, M.D. of Tucson, be deferred until the next meeting of this Board.

No action indicated in report received from AMA reiterating its support of the Blue Shield concept (Resolution No. 42, 1959 Clinical Session).

Public Relations Committee

It was moved by Doctor Steen, seconded by Doctor Dudley and unanimously carried that a sum of $100.00 be authorized paid to the National Society for Medical Research as a contribution of this Association toward its activity of protection of research institutions against sabotage by such groups as the anti-vivisectionists and a second area of creative development as represented by the National Conference on the Legal Environment of Medical Science.

OTHER BUSINESS

Arizona Medical School Study

Doctor Beaton reported on a recent meeting of the Arizona Medical School Study conducted by Joseph F. Volker, D.D.S., Director, to which members of the Medical School Committee of this Association were invited.

U. of A. Distinguished Service Awards

Doctor Beaton reported that Dermont W. Melick, M.D. and Samuel Wick, M.D. were the recipients of Distinguished Service Awards by the University of Arizona during its 75th Anniversary for extraordinary services rendered (Doctor Melick for service to the State; and Doctor Wick received it for his service in upgrading the Arizona State Hospital). The citations were very well done and will be published in Arizona Medicine, together with suitable photographs.

2% Sales Tax On Drugs

Referred by the Maricopa County Medical Society for consideration was a report setting forth certain facts concerning the 2% sales tax on drugs currently imposed, suggesting as a public relations project, that medicine spearhead a drive to repeal such taxation.

Doctor Beaton suggested that the Board of Directors might go on record as approving this stand of Maricopa County Medical Society and offering the cooperation of our Legislative Committee and Counsel, and the cooperation of the Woman's Auxiliary, in support of the repeal of this portion of the 2% sales tax imposed upon medicine.

The Board determined to approve Maricopa County Society's stand and offered the coopera-

tion of our Legislative Committee and legal counsel; and directed that our Auxiliary be informed that we support this matter of repealing the 2% sales tax on drugs and likewise urge its support.

Annual Meeting, 1961, Report

Doctor Smith as Chairman of the Scientific Assembly Committee reported on progress being made in the development of the Scientific program for the 1961 annual meeting. He stated that we have obtained the maximum number of speakers needed – eight – consisting of Doctor John H. Mulholland, New York University, surgeon; Doctor Evan Calkins, Massachusetts General Hospital, dermatologist; Doctor Herb Abrams, from Stanford, who is a heart research man; Doctor H. Corwin Hinshaw, whom you all know, chest diseases; Doctor Mahlon Delp of the Department of Medicine, Kansas; Doctor John W. Rebuck from the Ford Hospital, hematology; Doctor Victor A. Drill who is the head research man for Searle & Company and deals with the hormone control of kidney functions, etc.; and Doctor Robert T. Manning from the Research Department, University of Kansas.

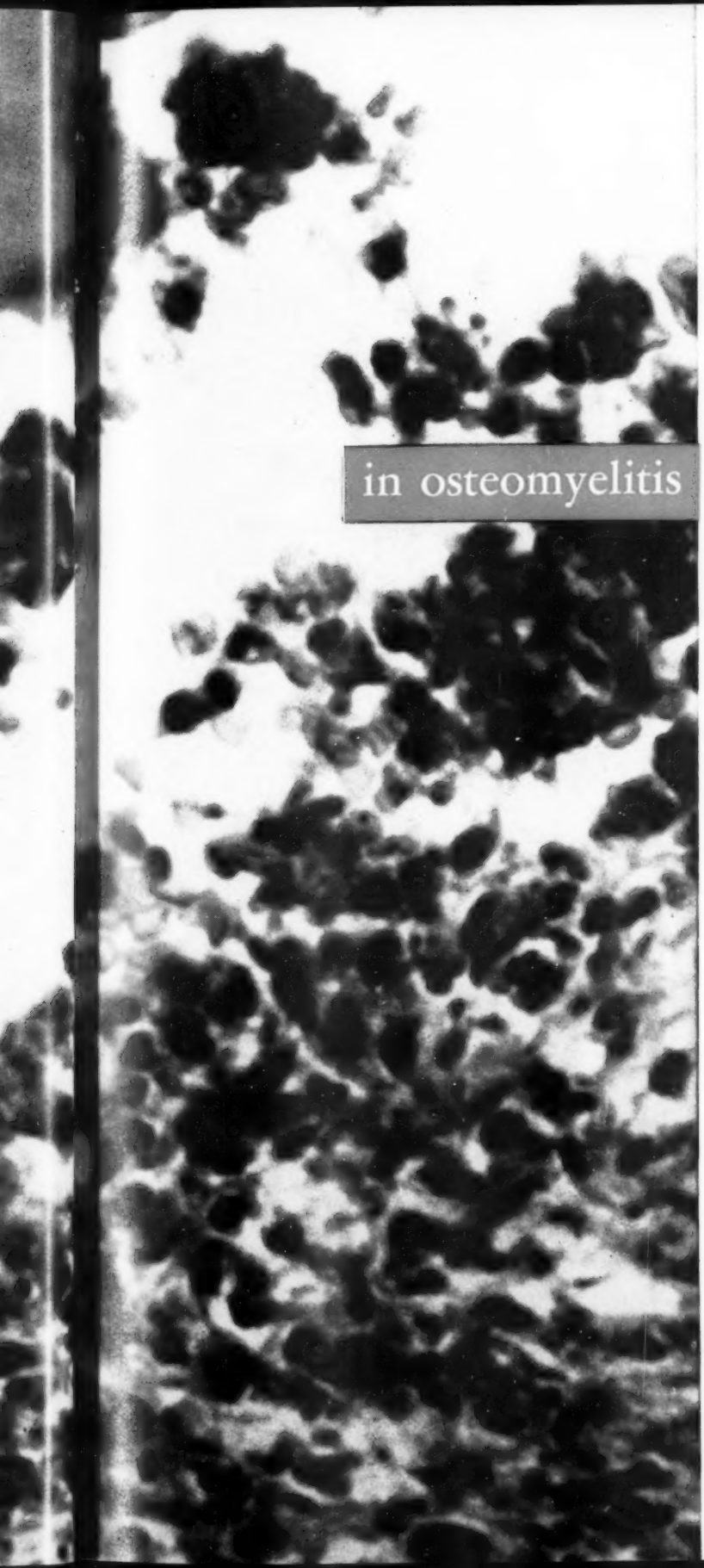
It was moved by Doctor Tuveson, seconded by Doctor Melick and unanimously carried, on recommendation of the Chairman of the Scientific Assembly Committee: that allied groups may be invited to attend the annual meeting banquet, to include possibly official representatives of the pharmaceutical, dental, registered nurses and practical nurses associations, be approved.

THE MEETING ADJOURNED AT 3:55 P.M.

Lorel A. Stapley, M.D.
Secretary
By Leslie B. Smith, M.D., President-elect
Acting Secretary

Since 1946, annual admissions in all hospitals have increased over 50 per cent; the number of employees has increased more than 75 per cent; and total expenditures have increased from just under $2 billion to more than $7 billion.
(American Hospital Association)

Bone section: erosion
and purulent exudate



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Supplied: Capsules, each containing Panmycin* Phosphate (tetracycline phosphate complex), equivalent to 250 mg. tetracycline hydrochloride, and 125 mg. Albamycin,* as novobiocin sodium, in bottles of 16 and 100.

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Occupational therapist guides patient in newly acquired hobby of making artificial flowers. All patients at Camelback Hospital are encouraged to participate in constructive hobbies as another integral part of their rehabilitation program, according to doctor's instructions. Hobbies may be pursued outdoors in the scenic recreation area or in the special hobby workshop in the hospital.

ocated in the heart of the beautiful Phoenix citrus area near picturesque Camelback Mountain, the hospital is dedicated exclusively to the treatment of psychiatric and psychosomatic disorders, including alcoholism.

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IN SINUSITIS, COLDS AND UPPER RESPIRATORY DISORDERS

NEW DIMETAPP® Extentabs®

LET YOUR PATIENTS BREATHE EASIER!

In sinusitis, colds and other upper respiratory and allergic disorders, new DIMETAPP Extentabs offer more useful decongestant therapy.

UNSURPASSED RELIEF OF NASAL CONGESTION: In DIMETAPP Extentabs, the unexcelled antihistamine, Dimetane, and two outstanding decongestants—phenylephrine and phenylpropanolamine—promptly dry secretions and reduce edema and congestion in the nose, the sinuses, and the upper respiratory tract.

CLEAR BREATHING FOR 12 HOURS ON 1 TABLET: Long-acting DIMETAPP Extentabs offer up to 12-hour relief on just one tablet. Easier-to-use DIMETAPP reaches into areas which nose drops or sprays can't touch—without rebound congestion.

EXCEPTIONAL FREEDOM FROM SIDE EFFECTS: DIMETAPP Extentabs are exceptionally free of side reactions. Dimetane offers a high percentage of relief with only drowsiness as a possible, infrequent side effect. Small, fully efficient dosages of decongestants minimize overstimulation.

DIMETAPP Extentabs contain Dimetane® (parabromdylamine [brompheniramine] maleate) 12 mg., phenylephrine HCl 15 mg., and phenylpropanolamine HCl 15 mg.

DOSAGE: Adults—1 Extentab q. 8-12 hours. Children over 6—1 Extentab q. 12 hours. Administer with caution to patients with cardiac or peripheral vascular diseases and hypertension, and to those sensitive to antihistamines. See package insert for further details and bibliography.

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ETHICAL PHARMACEUTICALS OF MERIT SINCE 1878

Trancoprin®

acetylsalicylic acid (300 mg.) and chlormezanone (50 mg.)

Tablets

a broad spectrum non-narcotic analgesic

Trancoprin, a new analgesic, not only raises the pain perception threshold but, through its chlormezanone component, also relaxes skeletal muscle spasm[1-6] and quiets the psyche.[2,3-5,7]

The effectiveness of Trancoprin has been demonstrated clinically[8] in a number of patients with a wide variety of painful disorders ranging from headache, dysmenorrhea and lumbago to arthritis and sciatica. In a series of 862 patients,[8] Trancoprin brought excellent or good relief of pain to 88 per cent of the group. In another series,[9] Trancoprin was administered in an industrial dispensary to 61 patients with headache, bursitis, neuritis or arthritis. The excellent results obtained prompted the prediction that Trancoprin "... will prove a valuable and safe drug for the industrial physician."[9]

Exceptionally Safe

No serious side effects have been encountered with Trancoprin. Of 923 patients treated with Trancoprin, only 22 (2.4 per cent) experienced any side effects.[8,9] In every instance, these reactions, which included temporary gastric distress, weakness or sedation, were mild and easily reversed.

Indications

Trancoprin is recommended for more comprehensive control of the pain complex (pain → tension → spasm) in those disorders in which tension and spasm are complicating factors, such as: headaches, including tension headaches / premenstrual tension and dysmenorrhea / low back pain, sciatica, lumbago / musculoskeletal pain associated with strains or sprains, myositis, fibrositis, bursitis, trauma, disc syndrome and myalgia / arthritis (rheumatoid or hypertrophic) / torticollis / neuralgia.

Dosage

The usual adult dosage is 2 Trancoprin tablets three or four times daily. The dosage for children from 5 to 12 years of age is 1 tablet three or four times daily. Trancoprin is so well tolerated that it may be taken on an empty stomach for quickest effect. The relief of symptoms is apparent in from fifteen to thirty minutes after administration and may last up to six hours or longer.

How Supplied

Each Trancoprin tablet contains 300 mg. (5 grains) of acetylsalicylic acid and 50 mg. of chlormezanone [Trancopal® brand]. Bottles of 100 and 1000.

Trancoprin Tablets / **non-narcotic analgesic**

References: 1. DeNyse, D. L.: *M. Times* 87:1512, Nov., 1959. 2. Ganz, S. E.: *J. Indiana M. A.* 52:1134, July, 1959. 3. Gruenberg, Friedrich: *Current Therap. Res.* 2:1, Jan., 1960. 4. Kearney, R. D.: *Current Therap. Res.* 2:127, April, 1960. 5. Lichtman, A. L.: *Kentucky Acad. Gen. Pract. J.* 4:28, Oct., 1958. 6. Mullin, W. G., and Epifano, Leonard: *Am. Pract. & Digest Treat.* 10:1743, Oct., 1959. 7. Shanaphy, J. F.: *Current Therap. Res.* 1:59, Oct., 1959. 8. Collective Study, Department of Medical Research, Winthrop Laboratories. 9. Hergesheimer, L. H.: An evaluation of a muscle relaxant (Trancopal) alone and with aspirin (Trancoprin) in an industrial medical practice, to be submitted.

Winthrop LABORATORIES, New York 18, N. Y.

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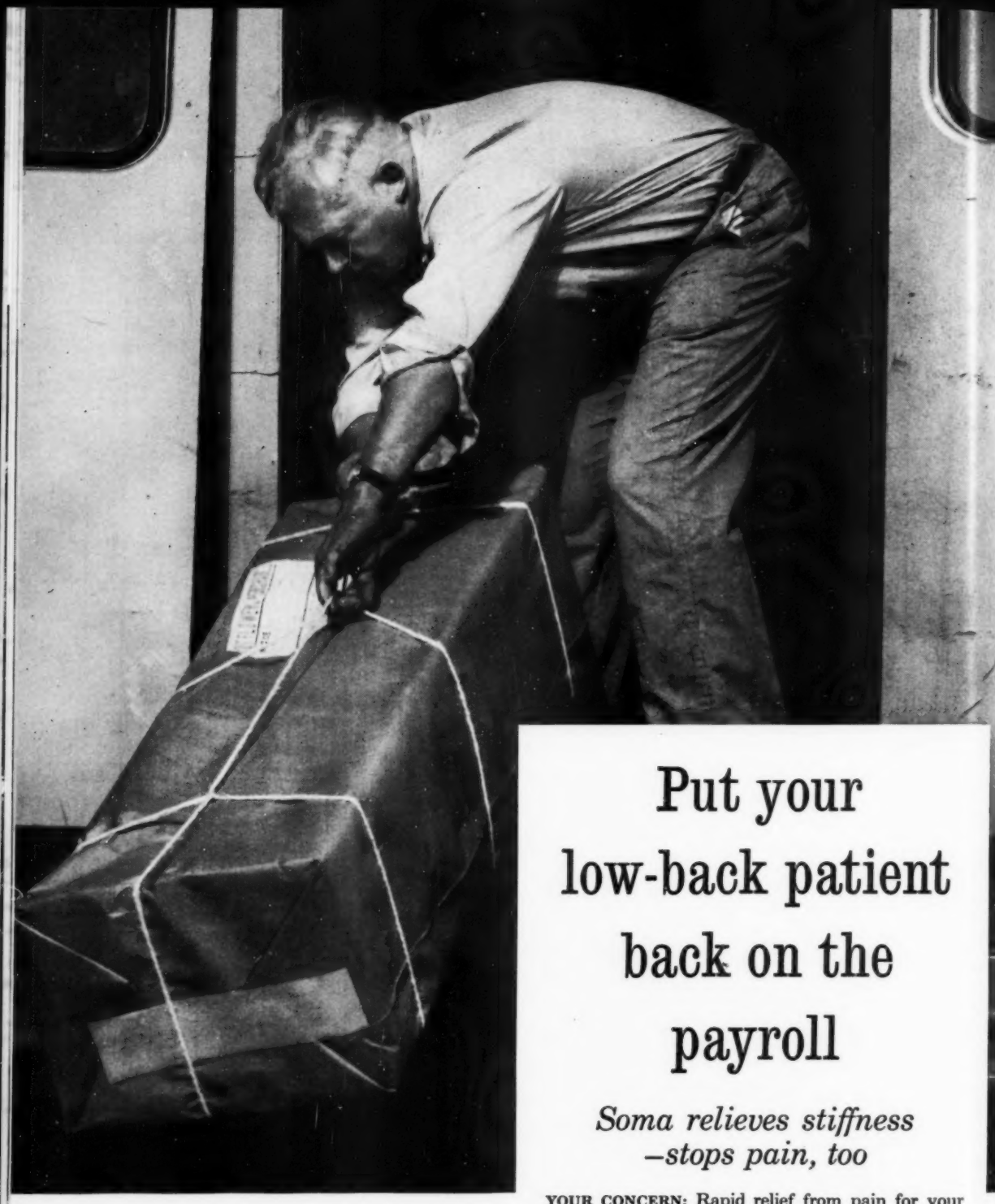

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Vol. 18, No. 1 January, 1961

Left Atrial Myxoma*

Meyer Markovitz, M.D.
and
Samuel R. Joseph, M.D.
Phoenix, Arizona

A patient with left atrial myxoma diagnosed ante-mortem is reported.
When present, the findings of changing signs and symptoms with change in position, and dyspnea but not orthopnea, is highly suggestive of an unusual disease, i.e., atrial myxoma.
Angiocardiography is the best diagnostic procedure for myxoma.
When myxoma is suspected, exploration and actual removal of the tumor is best accomplished by use of the open heart surgical technique.

MYXOMA of the atrium has been a post-mortem diagnosis until very recently. With the advent of open heart surgery making these tumors amenable to surgical extirpation there has been an upsurge of interest. As recently as June 1957 only 13 instances were found of the diagnosis of atrial myxoma during life. Eight were actually diagnosed and five others were found at operation for "mitral stenosis."(4) The following is a presentation of a patient with left atrial myxoma diagnosed ante-mortem.

A 46-year-old white male, was seen after the sudden onset of right hemiparesis. On the day of hospitalization, as he bent over to lift a box, he suddenly felt dazed, could not speak, and could not stand or use his right hand. Aside from the neurological findings, the physical examination revealed a palpable systolic thrill at the apex, and apical systolic and diastolic murmurs. The pulse rate was 80 with a regular rhythm, and the blood pressure was 118/70; the heart was not enlarged; the lungs were clear; the liver and spleen were not felt. The past history was significant in that this patient had been followed for a period of eight years and no murmur had ever been heard. There was no history of rheumatic disease. There was an episode of bronchial asthma 11 years previously. He was told that there was a heart attack with the asthma attack, however, he was only in the hospital a week and was then told there was nothing wrong with his heart. He had mild epigastric distress off and on for about five years.

His course in the hospital was one of gradual improvement in the right hemiparesis and motor aphasia and a progressive worsening of his cardiac status. At first, the diastolic murmur at the apex was rumbling in character and the first heart tone was loud and snapping with a presystolic accentuation. At various times, a loud api-

*Read at the Regional Meeting, American College of Physicians, Tucson, Arizona, December 12, 1959.

cal systolic murmur was also heard. An opening snap was heard by examiners. He felt much better lying down at a 25 degree angle or less rather than sitting upright. A chest x-ray showed development of an effusion in the small fissure on the right and later the heart appeared enlarged. The x-rays were puzzling in that on the first set the concavity produced by the barium-filled esophagus was on the left side. The second film showed the concavity on the right side. It was later determined that the first films were taken with the patient upright, and the second films, because of his illness, were taken in the supine position. He had two episodes in the hospital, noted by the nurses, when he suddenly became very short of breath, pulseless, and syncope ensued. He quickly recovered from both of these episodes.

A thoracotomy was performed two weeks after his admission to the hospital. Nothing was found in the mediastinum and the pericardial sac was also clear. A diastolic thrill could be felt in the region of the AV groove, and the heart action was noted to be extremely forceful. The pressure however was only 100 mm of Hg. systolic. The operator went ahead with exploration of the left atrium. On initial examination, he felt a soft mass beneath the aortic leaflet, but this disappeared and then later in the procedure a stalk-like structure could be felt arising from the deep posterior area of the left atrium. At this point, an attempt was made to palpate the pulses in the legs. When they were not found, a saddle embolus was suspected. An embolectomy was done at the aortic bifurcation and a grape-like mass was removed. Another similar embolus was removed from the subclavian artery, and another from the left brachial artery. At the completion of the intracardiac exploration, there was immediate improvement in the quality of the heart beat and the thrill which was palpated originally had disappeared. At the time the patient was transferred to the cart to return to his room, spontaneous respiration ceased. There was no change in the heart rate or blood pressure. He was placed in a respirator, but expired less than 24 hours later. The anatomical findings were myxoma of the left atrium, with a stump still present attached to the limbus of the foramen ovale; embolization of the right iliac artery; left subclavian artery; and left internal carotid artery with extension into the left middle cerebral artery. There were multiple infarctions of the kidneys, spleen, and heart, and collapse and congestion of the lungs.

DISCUSSION

Pritchard,(13) in a revienw of cardiac tumors up to 1951, described approximately 126 cases of atrial myxoma. At that time he stated that "tumors of the heart are rarely diagnosed before autopsy, largely because there is little knowledge of their natural history." "Surgical treatment of these neoplasms is virtually unheard of, and the present state of diagnosis is far behind the therapeutic possibilities." Metastatic tumors of the heart occur with approximately 20 to 40 times the frequency of primary growths and were found in 3.9 per cent of all cancers studied.(13) The primary tumors of the heart include myxoma, carcinoma, rhabdomyoma, angioma, fibroma, and hamartoma; with myxomas constituting about 50 per cent of all primary cardiac tumors. Approximately three-fourths of those reported have occcurred in the left atrium. McAllen,(8) in a review of 95 cases up to 1950, found that 77 occurred in the left auricle. The proportion of right atrial myxomas is greater than 25 per cent in recent reports, possibly due to the fact that a number of patients were found at cardiac catheterization. Almost all are attached to or overlie the fossa ovalis or its rim and are usually polypoid in nature.

Pritchard(13) considers the myxoma a true neoplasm. There are, however, still some adherents to the view that these masses are thrombii.(14 & 1). In one instance, tumor removed at operation was described by a pathologist as a "chicken fat clot".(1) More recently, a patient had a multicentric myxoma with tentacles attached to the limbus of the foramen ovale on the left, and a similar tumor growing from a cleft of the imperfect closure of the foramen on the right. In another instance the tumor mass had a complete covering of endothelial cells and cysts at the base.(2) These findings are not seen in thrombii. In any case, the pathologic picture of myxoma, whether true neoplasm or thrombus, is a well-recognized entity.

The natural history of these tumors is unknown although it would seem that most of them are of short duration. However, one patient is reported as having a murmur for 30 years, with

mitral stenosis being diagnosed for 11 years. After open heart surgery was performed and the myxoma was removed, no murmur was heard. (1) In another patient, a history of heart murmur of 43 years duration is reported, with the patient dying of other causes and the tumor found post-mortem.(17) MacGreger and Cullen(19) mention a report from India of a small myxoma found in the atrium of a stillborn infant.

The most common age of death due to myxoma is 40 to 60 years, however, the age range reported is from 4 to 83 years. In the past it was reported that females are involved three times as commonly as males. However, recent reports show a more equal sex incidence.

Of the 30 patients operated upon from 1951 through 1958,(4) the first survival was in 1955 with only a partial excision of the tumor being accomplished. Hypothermia was tried in six cases, five survived but three had complicating ventricular fibrillation. Nine patients were operated upon by means of the cardiopulmonary bypass technique and eight survived. Since in the 15 cases attempted by the closed technique, there are only two survivors, it is apparent that the cardiopulmonary bypass or hypothermia technique, preferably cardiopulmonary bypass, should be used in all such patients. The patient reported here, and a near duplicate recently reported by Buzze,(3) further show the danger of embolization and death due to attempted exploration of the left atrium. If atrial myxoma is suspected, the open heart technique should be used.

Diagnostic features of myxoma of the heart, whether left or right, may be defined under three headings:(1) (1) Cavitary obliteration, (2) occlusion of the valve orifice, and (3) arterial embolism. Cavitary obliteration causes dyspnea, arrhythmias, cardiomegaly, and congestive failure, which is characteristically rapid and progressive. These findings have led to the mistaken diagnosis of constrictive pericarditis or myocarditis. It has also been pointed out that although these patients are dyspneic, they sometimes are not orthopneic. Lying flat, or at a small angle, may lessen their dyspnea.

Occlusion of the valve orifice must be intermittent in order for life to continue, and leads to murmurs, syncopal episodes, and episodes of paroxysmal dyspnea. Change of the murmur with position change has been stressed. However, in one review(10) this change of the murmur with change in position was found in only seven of 30 patients. In 20 patients reported between 1951 and 1954(5) a change in the signs and symptoms with change in body position was reported in only two instances. The murmur is commonly apical, diastolic, and rumbling in character; but systolic murmurs are also heard. This one physical finding leads to the greatest difficulty in diagnosis as most patients are mistakenly considered to have rheumatic heart disease. The presence or absence of a history of rheumatic fever is of little aid in diagnosis. Patients with a history of rheumatic fever have had an atrial myxoma and it is well known that approximately half of the patients with rheumatic heart disease do not give a clear-cut history of rheumatic fever.

An opening snap has been reported in a patient with left atrial myxoma in whom, at postmortem, the mitral valve leaflets were found to be entirely normal.(1) An opening snap was heard in this patient and at the time was considered to be a factor against the diagnosis of myxoma. It seems apparent that thickened mitral leaflets are not essential in the production of an opening snap. Arterial embolism has been a common finding and has led to a mistaken diagnosis of subacute bacterial endocarditis. Embolism may be the presenting feature, as it was in this patient, and may not be immediately fatal.(11) A combination of left atrial enlargement on x-ray, a mitral diastolic rumbling mumur, and embolic phenomena; sometimes even splinter hemorrhages of the nailbeds, fever, gangrene of toes, and elevated sedimentation rate leads very easily to the diagnosis of subacute bacterial endocarditis. However, blood cultures have been uniformly negative. The reason for these systemic reactions is not clear, but may be due to degenerative changes in the tumor itself.(19)

Routine laboratory findings have not been particularly helpful in the diagnosis of atrial myxoma. The electrocardiogram and the routine chest x-rays, including those with barium filled esophagus, have not been of aid in the diagnosis. There have been unusual instances of the diagnosis of cardiac tumor at fluoroscopy, (14) the

calcified tumor being seen bouncing about in the heart. The only two laboratory procedures which have led to the diagnosis on a number of occasions have been cardiac catheterization in which right atrial myxomata have been found, and more particularly angiocardiography. In angiocardiography the differential diagnosis would include thrombus, and possibly aneurysm of the sinus of Valsalva presenting into the atrium. The difference in location of the tumor and of most thrombii should make the diagnosis possible, (15, 16) as the tumor is attached to the fossa-ovalis and is usually much larger.

This patient had a number of findings which favored the diagnosis of an unusual disease. First: he had been followed for a number of years and had never had rheumatic heart disease and never had a heart murmur. Secondly, he had an embolic episode without atrial fibrillation; third, he had the very peculiar situation in which he felt less dyspneic when he was lying down than when he was sitting up; fourth, the murmurs changed from day to day and from position to position. Of all these, the most important was the desire of the patient to lie flat or relatively flat even though he was quite dyspneic. It is difficult to describe a physiologic cause for this other than a changing degree of obstruction of the mitral orifice. There is no commonly accepted term for this type of dyspnea. Two suggestions are eupnea decubitus and platypnea. (18) The confusing factors were the finding of an opening snap which we now know can occur in atrial myxoma, and the very confusing picture on the x-ray in which the barium filled esophagus shows a concavity on the right on one day, and two days later on the left.

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FEDERAL MILLS BILL

Federal law resulting from the Mills Bill now permits additional federal funds to be used by the states, on a matching basis, for the improvement of their medical care for the aged programs.

Under this law, these new matching funds are available to the states for use in two categories of need: 1) those now on the public assistance rolls (OAS recipients), and 2) those who are *not* on public assistance but who are unable to pay their medicals bills from their own resources.

Pelvic Pneumoroentgenography

Melvyn H. Schreiber, M.D.
Captain, MC, USAH
Fort Huachuca, Arizona

Pelvic pneumoroentgenography is a safe, rapid, and dependable method of acquiring additional information regarding the physical condition of the female pelvic viscera in selected cases. It has an advantage over culdoscopy in that it may be performed on out-patients with ease; and utilizing the technique described, it requires the services of one operator and one assistant. It provides a permanent record of the condition of all of the pelvic viscera which may be viewed at leisure by more than one physician, and it lends itself to numerous variations for the detection and diagnosis of pelvic disease.

PELVIC pneumoroentgenography is the term applied to X-ray visualization of the female pelvic viscera after induction of pneumoperitoneum. It has been in use for 40 years as an adjunct in gynecologic diagnosis, and various more or less complicated techniques have been evolved for the performance of the examination. This paper describes a rapid, simple, safe, and effective method of inducing pneumoperitoneum, positioning the patient, and exposing appropriate films, together with some examples of the results of the procedure.

INDICATIONS AND CONTRAINDICATIONS

The indications for pelvic pneumography are few and include the following: (1) verification of suspicious findings on pelvic examination and elucidation of equivocal findings, particularly in hard-to-examine obese, tense, unco-operative, or virginal patients; (2) determination of the status of the pelvic viscera after surgical procedures when the extent of surgery is unknown; (3) determination of the presence and extent of lateral spread of pelvic tumors; (4) determination of the presence and degree of fixation of bowel loops to pelvic structures; and (5) to provide a permanent record of organ size, shape, and location for future reference, particularly in the case of pelvic neoplasms treated by radiation therapy. The examination is contra-indicated in very old and debilitated patients, in the presence of acute or subacute pelvic inflammatory disease, and in the presence of a tumor or mass which completely fills the pelvis.

MATERIALS

Equipment necessary for pelvic pneumography consists of a carbon dioxide dispensing de-

vice and materials needed for effecting peritoneal puncture under aseptic conditions (Figure 1). We have used the Tubaflator*, a device originally designed for performance of the Rubin test, with gratifying results. This instrument consists of a carbon dioxide reservoir from which the flow of gas is controlled by a sensitive needle valve, the volume of gas delivered being measured by the water displacement method; a built-in mercury manometer simultaneously registers the pressure. The unit utilizes readily available standard carbon dioxide cartridges.** An 18 to 20 gauge spinal needle with obturator and materials for cleansing and anesthetizing the skin at the puncture site complete the necessary equipment.

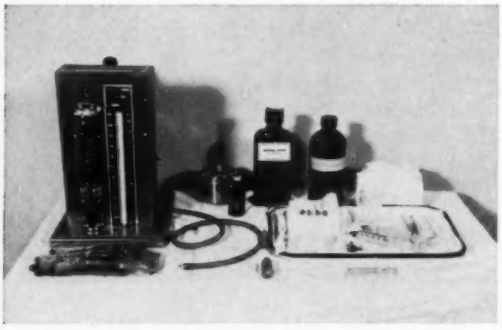

Figure 1
Equipment necessary for Pelvic Pneumography consists of a carbon dioxide dispensing device (Tubaflator, shown on the left) and materials needed for effecting peritoneal puncture under aseptic conditions.

PREPARATION OF THE PATIENT

The procedure is explained to the patient in detail to allay fear and ensure co-operation. A cleansing enema is administered about one hour prior to the examination, and the patient is asked to empty her bladder immediately before the examination is begun. The preceding meal is ordinarily withheld. We have not routinely used premedication of any sort. Rarely it has been necessary to administer a small dose of Demerol during the course of the examination in exceedingly anxious subjects for the relief of pain.

TECHNIQUE

Pneumoperitoneum may be induced in any of three ways: (1) trans-abdominally, (2) transtubally, or (3) through a culpotomy incision. We have had no experience with the last-named method and abandoned trans-tubal insufflation because of the longer time required, the greater discomfort to the patient, and the ease of performance of trans-abdominal induction.

The patient is placed upon the radiographic table, and after cleansing, painting, and draping the abdomen, a skin wheal is raised with 1 per cent procaine in the left lower abdominal quadrant. The tissues down to the peritoneum are then infiltrated with the anesthetic agent, following which an 18 to 20 gauge spinal needle, the obturator in place, is used to pierce the peritoneum. If the peritoneum has not been rendered insensitive the patient will experience a brief, sharp pain which aids the operator in determining the position of the needle tip. The obturator is then removed, and the extra-vascular, extra-intestinal, and extra-urinary position of the needle tip is verified by aspiration with a 10 cc syringe.

The rubber tubing leading from the gas cartridge chamber is then attached firmly to the hub of the needle, and introduction of the gas is begun. (Figure 2). 1000 to 1500 cubic centimeters are required for a satisfactory examination, and in most patients this can be introduced in 5 to 10 minutes. If the tip of the needle is properly placed the patient will usually experience mild discomfort in the epigastrium or in the flanks after 500-600 cc of gas are introduced, and if the patient's head is tilted up, manifest shoulder pain makes certain the correct placement of the needle tip. If the patient denies all discomfort during introduction of the gas, one must become

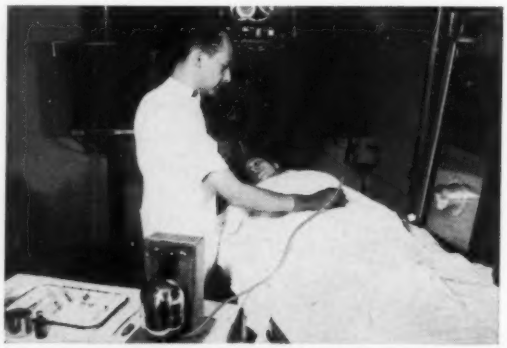

Figure 2
Trans-abdominal pneumoperitoneum is induced through a left lower quadrant needle puncture.

*Tubaflator obtained from the Thomas Instrument Company, P.O. Box 6605, Houston, Texas.

**Nitrous oxide gas may be used with equal safety; it has the advantage of being absorbed much more rapidly from the peritoneal cavity being 8 times more soluble in body fluids than CO^2. A tank source may be fitted with an appropriate volume measuring device for this purpose.

suspicious that no gas is entering the peritoneal cavity; a leak somewhere between the gas cartridge and the patient will usually be found under these circumstances. If the needle tip is inadvertently placed retroperitoneally or in the soft tissue of the abdominal wall, the pressure reading on the mercury manometer may rise steadily, and a reading over 120-150 mm of mercury should arouse the suspicion of this complication. After introduction of the gas the needle is removed and a small dressing placed over the puncture site.

The patient is then helped into a prone position and accurately positioned to the center of the table. With the shoulder brace in place to prevent the patient from slipping forward, the table is then tilted into a 30 degree Trendelenburg position. The radiographic tube is tilted 15 degrees towards the patient's feet, and the central ray is directed to the tip of the coccyx (Figure 3). A 36 to 40 inch focal-film distance is utilized. An 11 x 14 film is placed in the Bucky tray perpendicular to the long axis of the body, and the exposure is made.

Technical factors will vary with the size and the weight of the patient. Since contrast between the intra-peritoneal gas and the pelvic soft tissues is desired, deliberate underexposure is sought, and the following factors have proved satisfactory:

95-120 lbs.	80-90 kvp	10-15 mas
120-170 lbs.	90 kvp	25-35 mas
170-200 lbs.	90 kvp	35-45 mas

Because of the uncertainty in choosing precisely the optimum exposure factors for each patient, it has been our practice to expose three films in rapid succession, one using the factors suggested above, one with 10 to 15 more mas and one with 10 to 15 less mas. In patients with very large pelvic tumors it may be necessary to use much higher milliampere-second values in order to provide sufficient blackening on the film to entirely outline the mass. Ninety kilovolts should be sufficient for all, however.

After the films are exposed the table is returned to the horizontal level and the patient is permitted to assume any comfortable position. It is unusual for the patient to complain of discomfort sufficient to require medication once the upright position is assumed following completion of the examination. If shoulder pain is troublesome, aspirin or small doses of codeine usually provide relief. Assumption of the recumbent position with the hips elevated is also effective. Carbon dioxide is absorbed from the peritoneal cavity in 8 to 24 hours, and the patient's discomfort has almost always abated by the following morning.

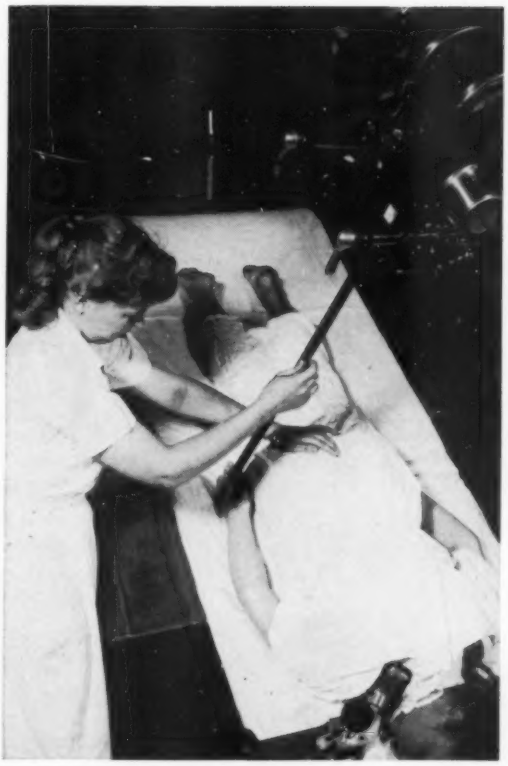

Figure 3
Following induction of pneumoperitoneum, the technician positions the patient in a 30° prone Trendelenburg position with the radiographic tube tilted 15° toward the feet and the central ray centered on the coccyx.

VARIATIONS

Any number of variations on this basic method may be applied. Oblique films, across-the-table lateral films, and decubitus films to demonstrate the thickness of the lateral pelvic walls may add additional information. Combined pelvic pneumoroentgenography and hysterosalpingography (gynecography) provides a comprehensive examination of the inner and outer contours of the pelvic viscera. The examination may be combined with excretory urography for demonstration of the relation of the ureters to the internal female genitalia, and other variations may be

used, depending on the indications.

COMPLICATIONS

Our experience with pelvic pneumoroentgenography has tended to confirm the numerous reports in the radiological and surgical literature of the harmlessness of the procedure. Many hundreds of examinations have been reported without bowel puncture, and if a careful technique is used the likelihood of peritonitis is exceedingly remote. The danger of gas embolism is small, carbon dioxide having been injected intravenous-

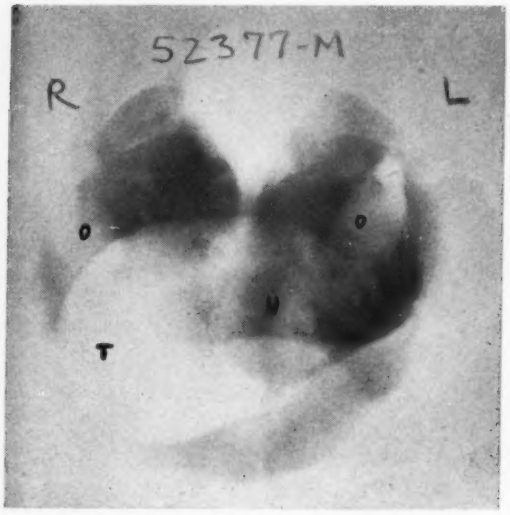

Figure 4
The uterus is assymetrically enlarged to the right, presumably because of a large leiomyoma. The ovaries are normal in size, shape, and position. O — ovary; U — uterus; T — tumor.

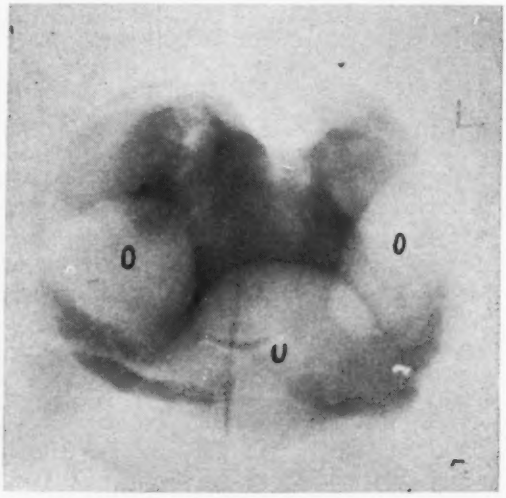

Figure 5
The patient is a 26-year-old obese female who had never been pregnant. After menarche at the age of 11 she experienced amenorrhea until age 21, following which she menstruated normally for 6 months, again becoming amenorrheic until the present. Pelvic examination was unsatisfactory because of the patient's obesity. Laboratory tests were within normal limits. Pelvic pneumography revealed a uterus of normal size and shape, with bilaterally and symmetrically enlarged ovaries. Pre-operative diagnosis was Stein-Levinthal syndrome. Operation on 4-3-58 disclosed normal uterus and tubes, with bilaterally moderately enlarged ovaries. Each ovary had a thick white capsule with numerous small subcapsular cysts. Wedge resection was done on both sides. Pathological examination confirmed the diagnosis of Stein-Levinthal syndrome. O — ovary; U — uterus.

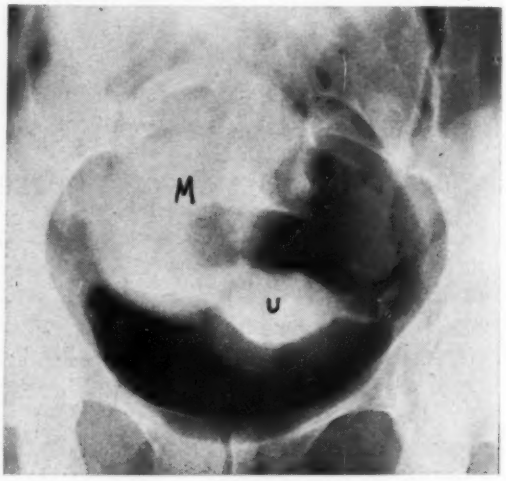

Figure 6
The patient is a 36-year-old female with no gynecological complaints. She had had bilateral tubal pregnancies in the past. Pelvic examination disclosed a moderately tender cystic fixed mass extending from the right pelvic wall to the uterus, the latter structure being displaced to the left. Pelvic pneumography showed a large right-sided rounded adnexal mass. Operation on 11-6-58 revealed a normal uterus and left adnexa. On the right a large inflammatory adnexal cyst was found with adhesions to the right oviduct and ileum. The pathological report was adnexal cyst with chronic inflammation and fibrosis. U — uterus; M — mass.

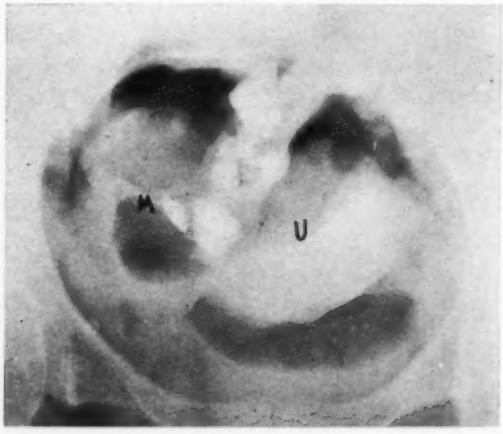

Figure 7
The patient is a 35-year-old female, gravida III, para III, with menorrhagia, urinary frequency, nocturia, dysuria. Pelvic examination revealed a tender 3 x 3 cm. right adnexal mass (6 x 7 cms. by another examiner). Pelvic pneumography showed a 6.5 x 8 cm. right adnexal mass which was thought to represent a tubo-ovarian abscess, uterine leiomyoma, or ovarian neoplasm. The left adnexal structures were poorly seen. Operation on 8-26-58 revealed mild pelvic inflammatory disease with adhesions and salpingitis on the left and an 8 x 5 x 3 cm. tubo-ovarian abscess on the right. U — uterus, slightly enlarged; M — mass; the superimposed opaque white densities represent residual barium in the recto-sigmoid.

ly for angiocardiography in man with no ill effects. Accidental introduction of 1000 cc of carbon dioxide into the subcutaneous fat of the abdominal wall in an exceedingly obese young woman was attended by no untoward effects. The transient discomfort usually experienced during introduction of the gas can almost always be tolerated by the patient without medication, and simple oral analgesics ordinarily control the short-lived shoulder pain which sometimes follows the procedure.

RESULTS

When successfully performed the following pelvic structures are usually visualized: (1) the uterus, seen as a transverse ovoid shadow 5-7 centimeters in width and 3-5 centimenters in length; (2) the uterine tubes, 3-6 millimeters in width; (3) the ovaries, small ovoid masses 2-4 centimeters in length and 1.5-3 centimeters wide; (4) the round ligaments, which may be distinguished from the oviducts by their anterior direction; (5) the bladder, a convex opacity between the uterus and the pubic symphysis, and (6) the rectum, an irregular soft tissue density just anterior to the sacrum. Because of some unavoidable size distortion, estimation of organ size is probably best accomplished by comparison with other pelvic viscera. For example, in the normal pelvic pneumogram the ovaries are seen to be approximately one-fourth the size of the uterus.

Uterine, tubal, and adnexal masses can be most effectively demonstrated by this technique. Figures 4, 5, 6 and 7 illustrate several conditions in which diagnostic pelvic pneumoperitoneum has proved helpful.

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Vascular Surgery and Abdominal Aortic Aneurysm

Report of case four and one-half years after aortic transplant

Matthew T. Moorehead, M.D.
Yuma, Arizona

Carl M. Frye, M.D.
Newark, Ohio

Report is made of a patient who not only lived four and one-half years after excision of an aneurysmal abdominal aorta, but also enjoyed relatively robust health during most of this period. The aneurysmal aorta was replaced by a youthful homograft that proved functionally satisfactory throughout. The patient's ultimate death was caused not by disease of his aorta but by hemorrhage from an intercurrent duodenal ulcer. It is gratifying to report this patient's excellent recovery and active life following the removal of a large segment of diseased aorta. The apparently atherosclerotic disease that developed within the homografted (15-year-old's) aorta seems peculiar and its metabolic significance is not understood, but such relatively rapid deterioration of a healthy young homograft might be regarded as further evidence in support of the current trend toward the use of artificial or synthetic grafts instead of homotransplants.

VASCULAR surgery has made tremendous strides during the past decade and is destined to make even greater progress during the next. With each advancement in understanding of living physiology and each improvement in technic, the difficult vascular operations become more practical. The use of artificial heart-lung technics (extra-corporeal circulation) makes the impossible seem routine. Surgery within an open, quiet, bloodless heart is an amazing sight to witness and its future possibilities seem almost unlimited.

Cardiovascular disease is our leading cause of death today and any measure that may lessen the loss of life from this source should be welcome to all. Even partial control of atherosclerotic disease will mean a further great increase in the already lengthened span of human life. Diet and chemistry may prove the final solution to this problem, but in the meantime other promising approaches should be encouraged. Arteriosclerosis is now the chief etiological factor in aneurysm of the aorta although formerly syphilis was quite important. The diagnosis of aortic aneurysm can often be made with little difficulty by ordinary means and without aortography. A large pulsating mass is readily palpable in most abdominal cases.

Surgical replacement of the abdominal aorta has proved successful only within recent years

ing an episode of immediate post-operative hem- and the literature on this subject is still quite limited. The usual operative technic includes complete occlusion (clamping) of the aorta just distal to the renal arteries for a variable period of time during which the diseased subjacent portion is removed and replaced by a homograft or prosthesis, thereby restoring the circulation to the lower half of the body. Complete interruption of the aorta is permissible for as long as two hours, if done distal to the renal arteries, but only for about twenty minutes, proximally. If the aneurysmal aorta proves unresectable, it may be bypassed or wrapped and supported by various agents, (polyethylene, teflon, dacron, ivalon, diacetyl phosphate, etc.).

Dubost (1951)(1) and Oudot (1953)(2) seem to have been amongst the first to successfully excise and replace the abdominal aorta, but DeBakey, Cooley and associates(3,4) began their epochal work at about the same time and are still quite active. Many others(5) have also contributed very much toward the solution of this difficult problem, particularly R. E. Gross. Recently Boyd and Pastel(6) reported twenty such cases in which fifteen were living after more than one year and only four still symptomatic; eleven had an entirely satisfactory outcome and six had no postoperative difficulties whatever. Their chief complications were vascular thromboses (five arterial, three venous) and bleeding from the anastomotic site. Injection of heparin into the common iliac arteries seemed to control the former and peritonealization the latter. The most exacting part of the technic seemed to be avoidance of the vena cava and duodenum.

The following report is of interest not only from a surgical standpoint but also from the viewpoint of pathologic physiology. The rapid development of an apparently atherosclerotic lesion in the transplanted 15-year-old's aorta seems quite unusual.

CASE REPORT

A tall, thin 66-year-old, white male developed during the year 1954, a large pulsating abdominal tumor mass that was promptly diagnosed as an aneurysm of the aorta, both by physical examination and by roentgenographic studies. The pulsating mass was readily palpable through the lower abdominal wall and was variously described by physicians as being the size of a "football" or small "watermelon". Concern was repeatedly expressed for the life of the patient in case of its rupture.

Fig. 1. Penetrating, exsanguinating duodenal ulcer (arrow) showing open blood vessel in floor of ulcer

In December 1954 the patient was referred to an expert vascular surgeon, to whom we are indebted for the privilege of reporting this case. After further diagnostic studies, an entirely successful operative excision of the huge abdominal aneurysmal mass was done by Robert M. Zollinger, M.D., Columbus, O. (12/27/54). The aorta was removed from a point just distal to the renal arteries to a point well beyond the aortic bifuraction. The diseased vascular mass was then replaced by a segment of normal aorta (homograft), that had been taken from the body of a boy aged 15 years who had just been killed in an automobile accident.

Following this extensive operation the patient's convalesence was was uneventful, except-

ing an episode of immediate post-operative hemorrhage that necessitated prompt re-exploration. The patient made a complete recovery within a few weeks and was soon able to resume work at his usual occupation as a gasoline-station attendant near our hospital. There he was repeatedly observed over a period of years doing real physical labor, and with no apparent difficulty (1955-1957).

Prior to his sudden death in December 1958, the patient had not been able to do heavy work for several weeks, but his general condition had been relatively good and he had been up and around as usual on the day preceding death. On the night of December 16, 1958 he awoke at about 4 A.M. feeling nauseated and dyspneic. He got up and went to the bathrom of his home, whereupon he vomited about a pint of dark-red blood and bloody fluid. He then collapsed to the bathroom floor and died before his wife could obtain assistance.

An autopsy, performed within a few hours, demonstrated an intact abdominal aorta, in good functional condition. An exsanguinating hemorrhage had taken place, not from the aorta but from an old, indurated, duodenal ulcer (Fig. 1). The ulcer had eroded into a sclerotic blood vessel and about 1000 ml of bloody fluid and blood clots were found within the lumen of the stomach. A similar quantity of bloody material was also present in the intestinal tract. The entire aorta was in relatively good functional condition. The homografted segment from the 15-year-old's aorta was in good condition as shown in the accompanying photograph (Fig. 2), but some odd intimal plaques of apparently atherosclerotic nature were noted. The aorta, proximal to the homograft was severely atherosclerotic and somewhat aneurysmal but functional. The common iliac arteries were also severely diseased and somewhat stenosed but still patent.

Microscopic study of the transplanted 15-year-old's aorta seemed to indicate that the homograft had undergone the usual partial replace-

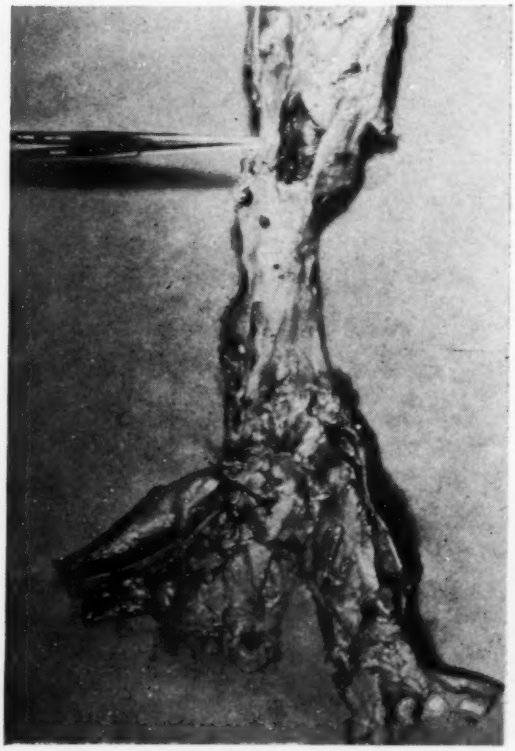

Fig. 2. Transplanted youthful abdominal aorta (center) with attached segment of older aorta (above) and common iliac arteries below.

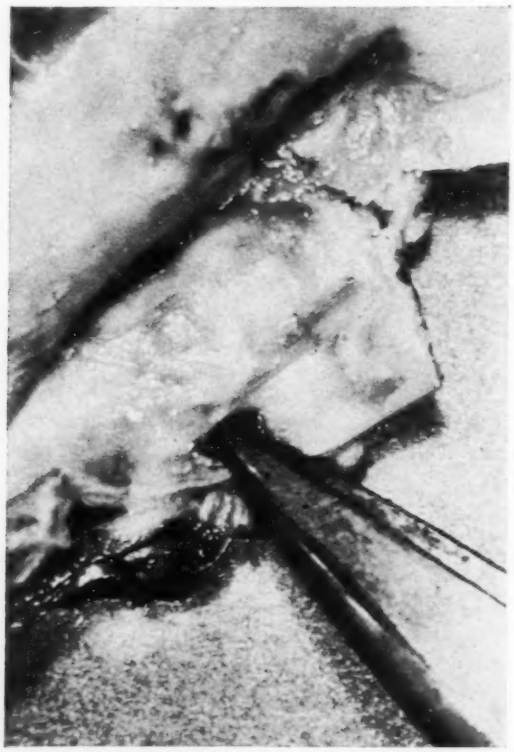

Fig. 3. Transplanted abdominal aorta (close up) showing central atheromatous plaques.

ment-necrosis and absorption, but also a senile type of intimal atherosclerosis. Atherosclerosis of this degree at the age of 15 years is quite unusual and suggests the presence of hormonal or chemical factors of some sort, circulating within the elderly atherosclerotic's bloodstream that predispose in some way to the formation of atherosclerotic plaques. Of course the transplanted aorta had been severed from its normal blood supply and therefore may have been hypersusceptible to atherosclerosis. The reaction of a host's bodily tissues toward a mass of transplanted tissue and foreign protein is seldom friendly and often quite hostile, but this probably does not fully account for the pathology noted here.

Parkview Hospital, Yuma, Ariz. (Dr. Moorhead).

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Studies on eight transplantable plasma-cell neoplasms of mice. Michael Potter and John L. Fahey, National Cancer Institute, Bethesda, Maryland. J. Nat. Cancer Inst. 24:1153-1165, 1960.

Summary — Eight plasma-cell neoplasms from mice of strain C3H/He or BALB/cAn, which were associated with the appearance of serum myeloma globulin in each new host, have been maintained in transplant. Each neoplasm was differentiated from the others by a characteristic serum- or urinary-protein electrophoretic pattern that developed during progressive growth of the transplanted tumor. The various plasma-cell neoplasms produced a variety of globulins with electrophoretic mobilities extending from the gamma to the alpha region. Each neoplasm produced proteins that were confined to a part of this globulin region, which indicates a restricted protein-producing capacity. Two neoplasms, which produced similar serum globulin electrophoretic patterns, were differentiated by the appearance of Bence Jones protein in the urine of mice bearing one of the neoplasms but not in mice bearing the other. During serial transplantation, or transplantation to hybrids and certain other strains, the characteristic serum- and urinary-protein changes remained constant and did not change. It was concluded that the globulin production unique to each tumor was a stable heritable characteristic.

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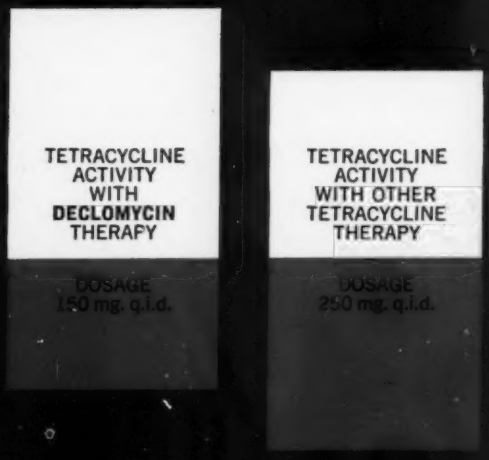

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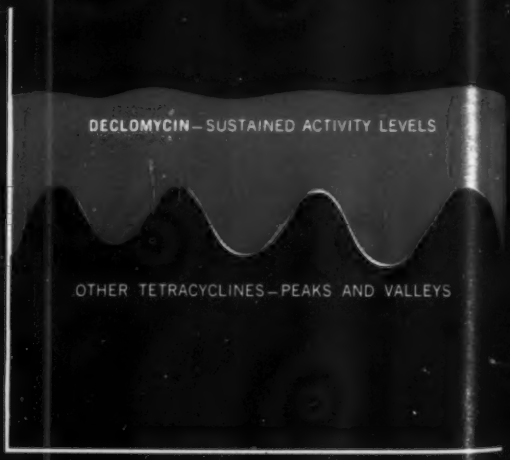

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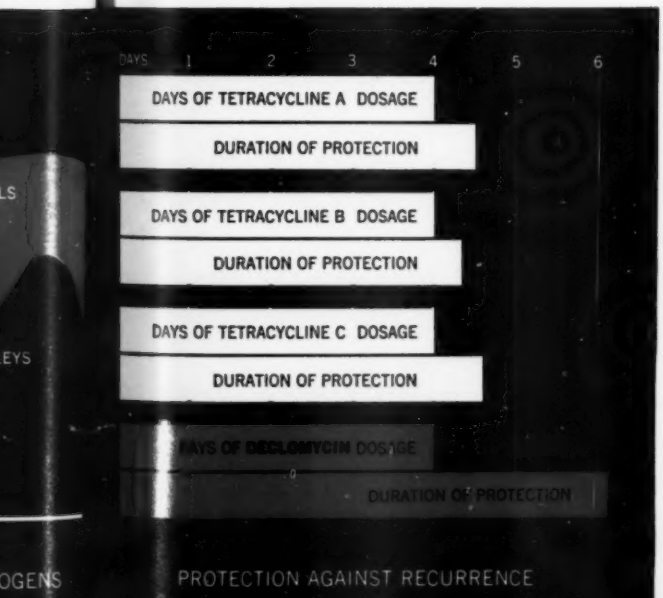

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The Present Status of Gold Therapy Phenylbutazone (Butazolidin) and The Chloroquines (Aralen, Plaquenil)*

L. Maxwell Lockie, M.D.
Professor and Head of the Department of Therapeutics
Medical School,
University of Buffalo

The intelligent uses of these drugs (gold salts, phenylbutazone (Butazolidin), and the chloroquines (Aralen, Plaquenil)), as part of the selected, individual, broad program of management mark further improvement in the treatment of arthritis, as they help to lessen the progression of the disease, and at the same time the patient is made more comfortable.

Gold Salts

GOLD salts, when combined into an overall complete program of treatment for patients with rheumatoid arthritis, is the most effective agent in our armamentarium to halt the progress of rheumatoid arthritis. Data(1) reveal that, in a large group of patients, 92 per cent experienced some degree of favorable response to therapy; 57 per cent of the group enjoyed a complete remission or showed major improvement. Gold sodium thiomalate was used routinely, gold thioglucose occasionally.

The antiarthritic action of gold salts is not yet understood. Objective evidence of improvement develops slowly, usually requiring at least six to eight weeks. First to appear is gradual abatement of the inflammatory phase of the arthritis, accompanied by a fall in the erythrocyte sedimentation rate. This is followed by lessening of pain and stiffness in the joint, and in a few weeks by improvement in general health. These results will continue over a long period but it is impossible to predict the degree to which they will progress. The drug is of greatest benefit in treating patients who have an active arthritic process, during the early or moderate stage of rheumatoid arthritis. Gold therapy should *not* be reserved for use as a last resort, for by then the period of its greatest usefulness is likely to be past. In recent years rheumatologists have come to prescribe gold as early as possible in the course of rheumatoid arthritis. It is especially beneficial in preventing further joint damage, as is noted in the study of our patients, only 7 per cent of whom failed to show measurable improvement.

In any one of several possibly coexisting conditions, e.g., acute disseminated lupus erythematosus, severe kidney or liver impairment, or pregnancy, gold is not to be prescribed. It can, however, be administered safely in the presence of peptic ulcer, mental disturbances, hypertension, or diabetes. Age alone is not a contra-indication, for children can be given gold in suitably reduced dosage over periods of years; the same applies to elderly patients, even those over the

*Presented at the Fourth Annual Meeting of the Medical Society of the United States and Mexico, December 4, 1959, Scottsdale, Arizona.

Some quotations taken from "Arthritis and Allied Conditions," published by Lea and Febiger, Philadelphia, edited by Joseph L. Hollander, M.D.

age of 80. In both of these widely separated age groups it has proved effective.

The gold salt is given intramuscularly at seven-day intervals, the initial dose consisting of 10 mg., the second dose of 20 mg., and thereafter a dose of 40 mg. each week. If no signs of sensitivity appear, treatment is continued until 500 mg. has been administered. At this juncture the future weekly dosage of gold is determined on the basis of the patient's clinical status. Individuals with moderate or severe arthritis usually require further weekly injections of 40 mg. until a total dosage of 800 mg. has been administered. The treatment is then carried on with 20 mg. per week for a variable period, depending on clinical improvement, before cutting down to 10 mg. weekly. Thereafter, doses of 10 mg. are given at varying intervals, determined by the patient's condition, until a final schedule of 10 mg. once every four weeks for an indefinate period is achieved.

At each visit, prior to injection, the patient is questioned concerning such early signs of sensitivity as glossitis, stomatitis, or dermatitis. A complete blood count and urinalysis are necessary every two weeks during the first six weeks of treatment. Later blood studies and urinalysis may be carried out at monthly intervals. The current weekly schedule of a moderate amount of gold has almost entirely eliminated the hazard of severe toxic reactions.

Evidence of Sensitivity

Many patients will have a mild glossitis, stomatitis, or dermatitis but, with a decrease in the amount of gold given at weekly intervals, these symptoms usually disappear. In this group, especially, the effectiveness of therapy is amazing. While these reactions are mild and do not require that gold be discontinued, the physician must watch carefully in order that the symptoms do not become more severe. If deemed advisable, the gold may be omitted temporarily for a few weeks and then resumed with a smaller dosage. Occasional patients may develop severe reactions, but the number of such individuals is small when compared with the large group whose rheumatoid arthritis can be treated uneventfully with weekly intramuscular injections of gold salts. Beside the commonly seen sensitivity manifestations of glossitis, stomatitis and mild dermatitis, clinicians have reported albuminuria, gastrointestinal upsets, eosinophilia, colitis, tracheitis, and purpura, all of which have been observed in our group. If albuminuria is mild and does not tend to become worse, gold salts are continued. The more serious gold reactions, which fortunately now are rare, are likely to occur only when the administration of gold salts is pushed incautiously despite the warning appearance of glossitis, stomatitis or dermatitis. Should a severe reaction develop, it can usually be controlled by stopping the administration of gold and starting promptly the vigorous use of antihistamines, corticosteroids, or corticotrophin. When the toxic manifestation is not easily controlled, the use of BAL (British anti-lewisite) will prevent further involvement. With reasonable supervision, gold salt therapy can be continued in many patients for years without significant difficulty.

Results

A total of 369 patients, each of whom was seen at weekly intervals for a minimum of at least three months (many have been followed for years) received a minimum of 300 mg. of gold salts intramuscularly, were compared with 566 controls. Patients in the control group received the same broad program of treatment, but instead of an injection of gold salts, they were given a weekly injection of streptococcus vaccine containing 4 million organisms. Of those treated with gold salts, only 7 per cent, as already stated, failed to show some improvement, whereas this was true of 13 per cent among the controls. In the group treated with gold salts 57 per cent experienced a complete remission or showed major improvement. This was in comparison with 38 per cent among the controls. Patients in a group receiving individually a total of less than 300 mg. of gold salts, however, showed no greater improvement than did those who were given no gold at all.

Conclusion

The above data confirm the clinical impression that gold salts given by intramuscular injection, as one vital component of a rounded, conscientiously followed program for the treatment of rheumatoid arthritis, afford patients a 20 per cent advantage in terms of a better chance of complete recovery or of major improvement. Modern gold salt therapy, wisely administered,

may be continued safely over a period of many years.

Evidences of mild sensitivity often do occur; however, they are usually readily controlled by decreasing the dosage or omitting a few doses of gold. Severe reactions develop in less than 1 per cent of patients and are combated with appropriate measures.

Thus, in the modern, many-sided therapy of rheumatoid arthritis, injectable gold salts have come to occupy a position of proved worth and demonstrated safety.

PHENYLBUTAZONE (BUTAZOLIDIN)

In 1949 a new anti-arthritic compound was introduced for therapeutic trial consisting of 15 per cent aminopyrine and 15 per cent phenylbutazone sodium. This product was given the name Irgapyrine in Europe and Butapyrin in the United States. It soon was evident that this drug was of value in the treatment of various arthritic conditions.

Pharmacological Action

Clinical response to phenylbutazone depends on its three major properties of analgesia, antipyrexia, and as an anti-inflammatory agent.

The absorption of phenylbutazone from the gastrointestinal tract is rapid and complete, the peak of plasma concentration being reached in two hours, whereas absorption from intramuscular injection is slow, with peak plasma levels 6-10 hours later. The only advantage of the intramuscular route of administration is a reduction of gastrointestinal effects. On repeated daily doses there is an accumulation of this drug in the body with a steadily rising concentration in the plasma until a plateau is attained by the third or fourth day. The plasma plateau level, a result of slow biotransformation at relatively low plasma levels, can be obtained in single daily doses or in divided doses. The plasma plateau level on the recommended therapetic dosage varies from 50 to 150 mgm per liter. After withdrawal of the drug, detectable quantities are present in the body for 7-10 days, or longer. This plateau which is constant for each patient, varies because of differences in individual rates of biotransformation averaging 15 to 25 per cent, daily. The half life of the drug in man is 72 hours. The plasma plateau level of any patient taking 1600 milligrams daily is not appreciably greater than at 800 milligrams daily. An increase in dosage will not result in added beneficial effect. Phenylbutazone has a much greater affinity for the plasma proteins than tissue proteins: so that about one-third of a single dose is localized in the plasma (which is only 5 per cent of the total body weight.)

Small amounts of two related compounds are found in the urine (with only traces of phenylbutazone per se). It is probable that they represent the major metabolic pathways since both these products are exteriorly metabolized when given intravenously.

Creatinine clearance studies indicate that glomerular filtration is not effected, but that decreased excretion of water and salt is due to increased tubular re-absorption. There are various drugs, such as demerol and morphine, whose intensity and duration of action are increased by phenylbutazone. This may be the result of a decrease in their urinary excretion. In fact, pretreatment with phenylbutazone doubled and tripled the intensity and duration of the analgesic effect. Phenylbutazone does appreciably alter the excretion of substances such as steroids, PAH, and urate which are influenced by protein binding.

Phenylbutazone has no known effect on endocrine balance. It does not cause a fall in adrenocortical ascorbic acid, alter urinary excretion of 17-ketosteroids, or effect either carbohydrate metabolism or insulin requirement, but typically reduces the elevated serum protein-polysaccharide ratio which accompanies inflammation. Reduction in the hematocrit seen during therapy with this drug is a result of its sodium and chloride retaining properties.

The indications for the use of phenylbutazone are many since it is valuable in treating other conditions as well as rheumatoid arthritis. The most spectacular results are obtained in patients who have rheumatoid spondylitis or gouty arthritis. Those with rheumatoid spondylitis derive marked benefit even with low dosage over long periods of time. This effect is far greater than that obtained by salicylates alone. These patients tolerate the drug well.

In acute gouty arthritis the relief of symptoms occurs in almost all patients using large amounts over a 24 to 48 hour period. An effective dosage is 200 mg. every 2 hours for 4 doses — to be repeated the next day, if necessary. No untoward effects have been observed in any of the patients with gouty arthritis using this plan of dosage.

It is suggested that the daily dose does not *exceed* 400 milligrams. With the limitations of this drug in treatment of rheumatoid arthritis, it frequently provides temporary relief to those not responding to other analgesics, but should be administered under strict medical supervision. The dosage used in adults should be the minimum required to control the symptoms of rheumatoid arthritis. If an initial dose of 600 mgm. per day is given, after two days the dose should be decreased to 400 mgm. daily for the next few days before gradually lowering to a maintenance dose of 100 to 300 mgm. per day. *It is important to emphasize if no improvement occurs after one week, the drug should be discontinued.*

Because of adverse side reactions phenylbutazone should not be used in the presence of:

1. Pre-existing edema
2. Cardiac decompensation
3. Peptic ulcer
4. Blood dyscrasias and severe anemia
5. In combination with other potent medications which would increase the hazards of toxic reaction.

This drug must be used with caution in the presence of:

1. Hypertension
2. Cardiac conditions other than decompensation
3. Hepatic damage
4. Renal insufficiency
5. Senescence
6. Drug sensitivities

Similar to all other potent anti-arthritic drugs, phenylbutazone causes adverse side reactions in a certain percentage of patients. At the present time there is no satisfactory method of anticipating serious complications with this drug and these reactions are not related to dosage or duration of treatment.

In view of the efficacy of phenylbutazone and considering the side effects of adrenal cortical steroids as well as other anti-rheumatic agents used today, this drug deserves a position of prominence in the treatment of rheumatoid arthritis. With proper indications and precautions, phenylbutazone can be an important adjunct in treating rheumatoid arthritis, however the greatest therapeutic results are noted in rheumatoid spondylitis and gouty arthritis.

CHLOROQUINES (ARALEN, PLAQUENIL)

Since 1953 increasing numbers of medical reports present data which indicate the chloroquine group of drugs (Aralen-chloroquine phosphate) (Plaquenil, hydroxy-chloroquine sulfate) possess antirheumatic properties. Experience has shown symptomatic improvement in rheumatoid arthritis is best attained when they are given continuously for a minimum period of six months. Two excellent double blind studies tend to support the clinical evidence thus reported. (5) (3)

PHARMACOLOGY

Chloroquine phosphate is rapidly and completely absorbed when taken orally. The daily ingestion of 500 mg. increases the blood plasma level gradually over a period of four weeks to a maximum of 0.2 per liter. When it is discontinued the blood plasma level falls to half in five days. The concentration in the liver, kidney and lung is 400-700 times that in the blood plasma. Parker and Irwin(10) attribute this to affinity for nucleoproteins and nucleates. 10 to 20 per cent is excreted in the urine. This can be considerably accelerated by acidifying the urine with ammonium chloride administered orally.

THE CLINICAL USE OF CHLOROQUINES

At the present time the chloroquines have been shown to possess antirheumatic effects with symptomatic improvement in some patients with rheumatoid arthritis, especially those patients who have a positive L.E. cell phenomena.

Chloroquine phosphate (Aralen) is given as a 250 mg. tablet at supper or bedtime. Some patients will develop side effects. However, when they subside with cessation of the drug, treat-

ment may be resumed with half the original dose and then, if well tolerated, the full dose of 250 mg. daily may be resumed. A few, 5-15% must discontinue the drug completely. Significant improvement is most likely to occur after six months continuous therapy.

Hydroxychloroquine sulfate (Plaquenil) is administered in two divided doses of 200 mgm. each daily for initial and maintenance therapy. Now this is preferred to chloroquine (Aralen) as there are only 50% of the toxic effects and certainly should be given to those intolerant to it. Bagnall(2) gave it to 28 patients unable to take prolonged chloroquine phosphate (Aralen) therapy. 17 had some degree of improvement or better, while 7 had significant side effects.

The chloroquines may be discontinued at any time without withdrawal phenomena. It is suggested that *they should not be given:*

1. With concomitant use of gold salt injections or with phenylbutazone (Butazolidin).

2. To patients who are sensitive to quinine.

3. To those who have psoriasis, or liver, kidney and lung diseases.

TOXICITY

Bagnall(2) reported 41% males and 64% females experienced some type of side effect during the daily ingestion of 250 mg. chloroquine phosphate (Aralen). Usually decreasing the dose was sufficient to control these side effects in this series in 32%, but in 5% males and 15% females it was necessary to discontinue the drug. Cohen and Calkins(3) found they had to discontinue it in one-third of their cases, Scherbel(12) in 7%, LaTona and Norcross(8) reported reactions in 41 of 145 patients and in 13 it was necessary to discontinue the drug due to:

Anemia and leukopenia	1
Blurred vision and corneal infiltration	2
Nausea and G.I. upset	3
Rash	4
Headache and dizziness	3

Skin lesions were the most common evidence of sensitivity. They were several varieties — maculopapular, purpuric, lichenoid or various other pleomorphic types. Usually several months of continuing therapy preceeded the onset of the skin lesion. Decreasing the dose usually was sufficient to control them, however, occasionally the drug had to be stopped.

Gastro-intestinal symptoms appeared in 15-25% consisting of varying degrees of anorexia, nausea, vomiting, burning in epigastrium or abdominal cramps. In these instances, usually administration with meals or decrease in dosage or both, would be sufficient to permit continued therapy without these symptoms.

There are several other side effects which occur occasionally. They consist of falling out of some of the hair, blanching in blonds or redheads, leukopenia, blurring of vision, neurologic or mental disturbances. Usually the chloroquine was stopped if these reactions occurred.

The reactions are 50% less with hydroxychloroquine sulfate, (Plaquenil.) Freedman(5) stated that none of the 50 patients studied had any toxic effects of significance while taking 300 mg. chloroquine sulfate daily for 2 years.

RESULTS

It is interesting to present the results of several reports in tabular style:

	No. of Patients	Major Improvement	Minor Improvement	No Improvement
Haydu(7)	28	22	5	1
Freedman*(5)	50	43	3	4
Cohen and Calkins**(3)	20	18		2
Rinehart —(11)				
adults	14	4	4	6
children	11	8		3
Fuld(6)	39	31		8
Scherbel(12)	60	36	20	4
Cramer(4)	123	95	15	13
Lockie et al/.(9)	124	59	28	37
Bagnall(2)	150	100		
LaTona and Norcross(8)	145	45		100

*Part a double blind study
**Double blind study

The chloroquine group of drugs possess anti-rheumatic effects for some patients with rheumatoid arthritis. Several more carefully controlled experiences with longer periods of observation are necessary to assess properly the anti-rheumatic activity of these drugs.

Estado Actual de la Terapeutica Por Oro, Felibulazona (Butazolidina) y las Cloroquinas

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El uso inteligente de estas drogas (sales auricas, butazolidina y las cloroquinas: Aralen y Plaquenil), como parte de un tratamiento individual, selectivo e intergral, constituye un marcado avance en el tratamiento de la artritis, previniedo el progreso de la enfermedad trayendo al mismo tiempo el alivio tan deseado por el paciente.

Las Sales De Oro

Cuando se aplican a un programa integral de tratamiento a pacientes con Artritis Reumatoide, constituyen uno de los agentes más efectivos en el armamentarinm médico para contener el progreso de esta enfermedao Las estadisticas demuestran que de un grupo considerable de enfermos el 92% experimento una respuesta favorable en cierto grado al tratamiento; el 57%, tuvieron una remision completa a mejoraron notablemente. Se usó de rutina el Tiomalto Sódico; la Tioglucosa áurica ocasionalmente.

La acción antiartrítica de las sales de oro no está bien aclarada. La mejoría gradual as evidente requiriendo habitualmente de seis a ocho semanas. Lo primero en aparecer es el abatimiento de la fase inflamatoria de la artritis acompánada de una baja de la sedimentación globular. Esta es seguido por disminución del dolor y de la rigidez en la articulación; y en unas pocas semanas por mejoria en el estado general. Este resultado continuará por un largo período de tiempo, pero es imposible predecir hasta que grado progresará. La droga es altamente benéfica cuando se trata de pacientes que tienen un proceso activo de artritis, durante el estado primitivo o moderado de la artritis reumatoide. La Auroterapia no deberá reservarse para usarse como ultimo recurso, porque para entonces el período de su máxima utilización habrá pasado. En los ultimos años los reumatologos han venido recetando oro, tan tempranamente como sea posible, en el curso de una artritis reumatoide. Esto es especialmente benéfico en la prevención de futuro daño en la articulacion, como ha sido marcado en el estudio de nuestros pacientes, en quienes unicamente el 7 por cientó no presento una mejoría perceptible.

En cualquiera de las varias posibles condiciones coexistentes, tales como; lupus eritemato – sus agudo diseminado, grave deterioramiento del rinón o del Hígado, o embarazo, el oro no será recetado. Esto puede, como quiera que sea, ser administrado sin peligro, en presencia de ülcera péptica, disturbios mentales hipertensión o diabetes, La edad sola, no es una contraindicación; para niños el oro puede ser dado en dosis reducidas por periodos de años; lo mismo se aplica para pacientes ancianos, incluso aquellos que sobrepasan de los 80. En ambos de estos grupos ha probado su efectividad.

Las sales de oro son dadas intramuscularmente a intervalos de siete dias, la dosis inicial es de 10 mg., la segunda es de 20 mg. y después una dosis de 40 mg. cada semana. Si no aparecen signos de sensitividad, el tratamiento es continuado

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*Este trabaio fue presentado en la cuarta asamblea anual de la Asociation Medica de los Estados Unidos y Mexico el dia 4 de Diciembre de 1959, Scottsdale, Arizona.

**Traduccion al espanol por el doctor Carlos V. Greth, Phoenix, Ariz.

hasta que hayan sido administrados 500 mg. Al llegar a este momento, la futura dosificación semanal de oro es determinada sobre las bases del estado clinico del paciente. Los individuos con artritis moderada o severausualmente requieren mas inyecciones semanales de 40 mg. hasta que ha sido administrada una dosis total de 800 mg. El tratamiento es entonces Ilevado con 20 mg. por semana por un período variable, dependiendo de la mejoría clínica, antes de reducir la dosis a 10 mg. semanales. Mas adelante, dosis de 10 mg. son dadas a intervalos variables determinados por las condiciones del paciente hasta que un programa final de 10 mg. cada 4 semanas es ejecutado por un período indefinido.

En cada visita, siguiente a la inyección, el paciente es preguntado concerniente a a quellos tempranos signos de sensitividad como glositis, estomatitis o dermatitis. Una completa cuenta globular y análisis de orina son necesarios cada 2 semanas durante las primeras seis semanas de tratamiento. Subsecuentes estudios de sangre y orina deben ser hechos a interválos mensuales. El presente programa semañal de cantidades moderadas de oro, ha casi eliminado enteramente el peligro de reacciones tóxicas severas.

Evidencias de Sensitividad:

Muchos pacientes tendrán moderado glositis, estomatitis o dermatitis pero, con una disminución en la cantidad de oro dada a intervalos semanales, esos síntomas usualmente desaparecen. Especialmente en este grupo la efectividad de ésta terapéutica es asombrosa. Aun cuando reacciones son moderadas y no requieren que el oro sea discontinuado, el paciente debe ser cuidadosamente supervisado por el médico para que los síntomas no vengan a ser más severos. So se juzga conveniente, el oro puede ser omitido temporalmente por unas pocas semanas y entonces empezado con una dosis más pequeña. Ocasionalmente algunos pacientes pueden desarrollar severas reacciones, pero el nümero de esos individuos es pequeño, comparado con el gran grupo de enfermos con artritis reumatoide que pueden ser tratados con inyecciones semanales de oro, sin evidencia de sensitividad. Junto a las manifestaciones de sensitidad comunmente vistas, como glositis, estomatitis y dermatitis algunos clínicos han reportado albuminuria, trastornos gastrointestinales, eosinofilia, colitis, traqueitis y pürpura; todas ellas vistas también en nuestro grupo. Si la albuminuria es moderada y no tiende a aumentar, las sales de oro son continuadas. Las más serias reacciones, las cuales afortunadamente son raras ahora, probablemente ocurren solamente cuando la administración de sales do oro es aplicada imprudentemente a pesar de la presencia de glositis, estomatitis o dermatitis. Cuando se desarrolla una reacción severa, puede ser controlada usualmente, suspendiendo la administración de oro y empezando un pronto y vigoroso uso de antihistamínicos, corticoesteroides o corticotrofín. Cuando las manifestaciones tóxicas no son fácilmente controladas, el uso de BAL (British anti-lewisite) prevendrá futuras complicaciones.

Con razonable supervision la terapéutica con sales de oro puede ser continuada en muchos pacientes, por años, sin dificultades.

Resultados:

Un total de 369 pacientes cada uno de los cuales fué visto a intervalos semanales por un plazo no menor de 3 meses (muchos han sido seguidos por años) recibió un mínimo de 300 mg. de sales de oro intramuscularmente, y fueron comparados con 566 controles. Pacientes en el grupo control recibieron el mismo amplio programa de tratamiento, pero en vez de una inyección de sales de oro se les aplicó una inyección semanal de vacuna estreptocóccia conteniendo 4 millones de organismos. De esos tratados con sales de oro, solamente 7 por ciento como fué dicho, falló en presentar alguna mejoriá, mientras que en el grupo control fue 13 por ciento. En el grupo tratado con sales de oro, 57 por ciento experimentó una completa remisión, o mostró una gran mejoría. Esto fué en comparación con 38 por ciento entre el grupo control. Pacientes dentro de un grupo recibidiendo individualmente un total de menos de 300 mg. de sales de oro, como quiere que sea, no mostró mayor mejoría que aquellos a quienes no les fué dado oro para nada.

Conclusión:

Los datos anteriores confirman la impresión clínica que oro, dado por inyección intramuscular, como un vital componente de un redondeado y concienzudo programa seguido para el tratamiento de artritis reumatoide, produce pacientes un 20 por ciento, ventajoso en términos de mejor

oportunidad de completa recuperación o gran mejoría. La moderna terapéutica con oro, hábilmente administrada, puede ser continuada sin riesgo por un período de muchos años.

Evidencias de moderada sensitividad ocurren frecuentemente, como quiera que sea, son usualmente controladas disminuyendo la dosis o omitiendo unas pocas dosis de oro. Severas reacciones desarrollan en menos de 1 por ciento de los pacientes y son combatidas con medidas apropiadas.

Así en la moderna polifacética terápia de artritis reumotoide las sales de oro inyectables han venido a ocupar una posición de probado mérito y demostradaseguridad.

PHENYLBUTAZONE (BUTAZOLIDIN)

En 1949 un nuevo compuesto anti-artrítico fue introducido para ensayo terapéutico consistente de 15 por ciento aminopirina y 15% fenilbutazona de sodio. Este producto recibió el nombre de Irgapyrina en Europa y Butapyrina in los Estados Unidos. Pronto fue evidente que esta droga era de valor en el tratamiento de varias condiciones artríticas.

Acción Farmacológica:

La respuesta clinica a la fenilbutazona depende de sus tres mayores propiedades de analgésia, antipirexia y como un agente antinflamatorio.

La absorción de la fenilbutazona por a vía gastrointestinal es rápida y completa, el máximo de concentracion plasmática es alcanzado en 2 horas, mientras que la absorción por la via intramuscular es lenta, con máxima concentración plasmática 6 a 10 horas mas tarde. La ünica ventaja de la administración por viá intramuscular es una reducción de efectos gastrointestinales. En repetidas dosis diarias hay una acumulación de esta droga en el cuerpo con una sostenida elevación en la concentración plasmática hasta que una meseta es alcancanzada al tercer o cuarto día. El nivel de meseta plasmática, un resultado de lenta bio-transformación a relativamente bajos niveles plasmáticos, puede ser obtenida con una sola dosis terapeütica recomendada, varía de 50 a 150 mgm. por litro. Desqués del suspendimiento de la droga, perceptibles cantidades están presentes en el cuerpo por 7-10 dias, o más. Esta meseta la cual es constante para cada paciente, varia debido a diferencias individuales en la capacidad de bio-transformación promediando 15 a 25 per ciento diariamente. La vida media de la droga en el hombre es de 72 horas. El nivel de meseta plasmático de cualquier paciente recibiendo 1600 mg. diariamente, no es mayor que recibiendo 800 mg. diarios. Un aumento en la dosis no resultará en aumento del efecto benéfico. La fenilbutazona tiene mucho mayor afinidad por las proteínas plasmáticas que por las proteínas tisulares: así que aproximadamente un tercio de una simple dosis es localizada en el plasma (el cual es sólamente 5 por ciento del peso corporal total).

Pequenas cantidades de estos dos compuestos se encuentran en la orina (con solamente trazas de phenylbutazone). Es probable que ellos representan los mayores cursos de su metabolismo ya que ambos son metabolizados exteriormente cuando se les administra por vía intravenosa.

Los estudios de eliminacion de creatinina indican que la filtracion glomerular no es afectada sino que la evcrecion reducida de agua de sales es debida a un aumento en la reabsorción tubular. Hay varias drogas como el demerol y la morfina, cuya intensidad y duración son aumentadas por la butazolidina. Esto puede ser el resultado de una disminución en su excreción urinaria. De hecho un pretratamiento con butazolidinia altera apreciablemente la excreción de substancias como los esteroidos PAH, y uratos que son influenciados por enlace proteínico.

La butazolidina no tiene efecto conocido en el balance endocrino. No causa descenso en el ácido ascórbico adrenocortical ni altera la excreción urinaria de los 17-Cetosteroides ni afecta tampoco el metabolismo de los carbohidratos ni el requerimiento de insulina pero reduce típicamente los compuestos del suero proteino-polisacáridos que acompañan a la inflamacion. La reducción en el hematocrito que se observa durante la terapia con esta droga es el resultado de sus propiedades retentivas de Sodio y cloruros.

Las indicaciones para el uso de la butazolidina son muchas ya que tiene incalculable valor en el tratamiento do muchas enfermedades asi

como en la artritis reumatoide. El resultado mas espondilitis reumatoide o artritis gotosa. Aquellos con espondilitis reumatoide obtienen marcados beneficios hasta con bajas dosis por largos períodos de tiempo este efecto es mucho mayor que el que se obtiene con salicilatos solos. Estos pacientes toleran bien la droga.

En artritis gotosa aguda el alivio de sintomas ocurre en casi todos los pacientes usando grandes cantidades sobre un periodo de 24 a 48 horas. Una dosis efectiva es 200 mg. cada 2 horas por 4 dosis que será repetida el dia siguiente si es necesario. No han sido observados efectos desfavorables en ninguno do los pacientes con artritis gotosa usando este plan de dosificación se usa.

Es de sugerir que la droga *no exceda* de 400 mg. Con las limitaciones de esta droga en el tratamineto de artritis reumatoide frecuentemente provee alivio temporal a aquellos que no responden a otros analgésicos; pero debe ser administrada bajo estricta supervisión médica. La dosis usada en adultos debe ser la mínima requerido para controlar los sintomas de artritis reumatoide. Si es dada una dosis inicial de 600 mg., después de dos dias debe ser reducida a 400 mg. diariamente por unos pocos dias, antes de bajarla gradualmente a lo dosis de mantenimiento de 100 a 300 mg. por dia. *Es de suma importanica enfatizar que si no hay mejoria despues de una semana, esta droga debe de ser suspendida.* Debido a las adversas reacciones colaterales fenilbutazona no deberá ser usada en presencia de:

1. Edema pre-existente.
2. Descompensación cardiaca.
3. Ulcera péptica.
4. Discracias sanguíneas y marcada anemia.
5. En combinación con otras medicaciones potentes que pudieran aumentar los riesgos de reacción tóxica.

Esta droga deberá ser usada con precaución en presencia de:

1. Hipertensión.
2. Otras condiciones cardiácas (Descompensación ya fué nombrada arriba).
3. Lesión hepática.
4. Insuficiencia renal.
5. Vejéz.
6. Sensitividad a la droga.

Como todos las otras potentes drogas antiartríticas, la butazolidina causa adversas reacciones colaterales en un cierto porcentaje de pacientes. Hasta el tiempo presente, no hay un método satisfactorio de anticipar serias complicaciones con esta droga y estas reacciones no están en relación con la dosis o la duración del tratamiento.

En vista de la eficacia de la butazolidina y considerando les efectos colaterales de los adrenocorticoesteroides así como de otros agentes antireumáticos usados hoy en dia, esta droga reserva una prominente posición en el tratamiento de artritis reumatoide. Con apropiadas indicaciones ye precauciones la butazolidina puede ser un importante acosiado en el tratamiento de artritis reumatoide ya que el más grande resultado terapéutico es notado en espondilitis reumatoide y artiritis gotosa.

CLOROQUINAS. ARALEN.

Desde 1953, un nümero crecido de reportes médicos indican que el grupo de las cloroquinas (Aralen-fostato de cloroquina) (el plaquenil, sulfato de hidroxiclo-roquina) posee propiedades antireumaticas. La experiencia ha demostrado que cuando estas drogas se administran continuamente por un período no menor de 6 meses, se obtienen los mejores resultados.

FARMACOLOGIA

El fosfato de cloroquina es rapidamente y completamente absordido cuando se administra por vía oral. La diaria ingeshinó de 500 mg. aumenta el nivel sanguineo gradualmente por un periodo de 4 semanas a un máximo de 0.2 por litro. Cuando se para su administración, el nivel sanguineo baja a la mitad en 5 días. La concentración en el hígado, en el riñon y en el pulmon es 400 o 700 veces mayor que en el plasma. Parker e Irwin atribuyen esto, a una afinidad para las nucleoproteinas y los nucleótidos. Del 10 al 20% se elimina en la orina. La eliminación por la vía urinaria se puede acelerar notablemente, acidulando la orina con cloruro amónico administrado por la vía oral.

EL USO CLINICO DE LAS CLOROQUINAS

Actualmente, se ha comprobado que las cloroquinas tienen efectos antireumáticos y que producen mejoría sintomática en algunos casos de artritis reumatoide, particularmente en aquellos enfermos en que se manifiesta el fenómeno L.E.

El fostato de cloroquina (Aralen) se da porla via oral en una dosis de 250 mgms. con la cena o al acostarse. Algunos enfermos manifiestan reacciones. Sin embargo, cuando desaparecen al descontinuar la droga, el tratamiento puede seguirse reduciendo la dosis a la mitad. Un porcentaje de un 5 al 15% tienen que parar la administración completamente. Una mejoría significativa aparece casi con seguridad después 6 meses de tratamiento continuo.

El plaquenil, es administrado en 2 dosis diarias de 200 mg. como tratamiento inicial y de sostenimiento. Esta droga se prefiere al aralen, ya que sus efectos tóxicos son el 50% del aralén y debe administrarse a las personas que no toleran el aralén. Bagnall lo administró a 28 enfermos que no podian continuar con un tratamiento prolongado de aralén; 17 de ellos mejoraron y 7 tuvieron toxicidad.

Aunque se puedo suspender la administración de las cloroquina sin efectos desagradables, se susiere que no seden:

1. Cuando se usen sales de oro o concomitantemente con butabolidina.
2. A pacientes con intolerancia a la quinina.
3. A enformes con soriasis, a enfermos del riñon o del hígado.

TOXICIDAD

Bagnall reportó que un 45% de hombres y un 64% de mujeres, experimentaron efectos toxícos en mayor o menor grado al administrarseles 250 mg. de Aralén. Habitualmente, decreciendo la dosis fue posible controlar en estos grupos ed 32% de ellos, pero hubo necesidad de suspender la droga en un 5% de los hombres y en un 15% de las mujeres. Cohen y Calkins encontraron que tuvieron que suspender la droga en una tercera parte de los casos. Scherbel suspendió la droga en un 7% de los casos, LaTona y Norcross en 41 de 145 pacientes reportaron reacciones y en 13 fue necesario descontinuar la droga debido a:

Anemia y lecuopen a.....1
Trastornos visuales e infiltración corneal 3
Nausea y molestias G-I 3
Erupción cutánea 4
Cefalea y vértigo 3

Las lesiones dermatológicas fueron las reacciones mas evidentes de hipersensibilidad. Fueron de varios tipos: máculo-papulares, purpúricas, liquenoides y otros. Generalmente aparecieron después de varios meses de administración de la droga y solo fue necesario disminuir la dosis para su control habiendo algunos casos en que se tuvo que suspender la droga.

Los síntomas gastrointestinales aparecieron en un 15-25% de los casos consistiendo en anorexia, nausea, vómito, ardor epigéstrico y calambres abdominales. En estos casos, la administración con las comidas o reduciendo la dosis permitió continuar el tratamiento.

Hay otros síntomas de toxicidad que ocurren ocasionalmente. Consisten en caida del pelo, encanecimiento, leucopenia, trastornos visuales y algunos trastornos neurológicos o mentales. La cloroquina se suspende habitualmente en estos casos.

Las reacciones son el 50% menos con el plaquenil. Freedman anoto que de 50 pacientes estudiados, ninguno presentó trastornos tóxicos de signifacación tomando 300 mg. de plaquenil diariamente por 2 años.

RESULTADOS

	No. de Pacientes	Mejoria notable	Menor mejoria	No mejoria
Haydu	28	22	5	1
Freedman	50	43	3	4
Cohen & Calkins	20	18		2
Rinehart:				
Adultos	14	4	4	6
Ninos	11	8		3
Fuld	39	31		8
Scherbel	60	36	20	4
Cramer	123	95	15	13
Lockie et al	154	59	28	37
Bagnall	150	100		
LaTona y Narcross	145	45		100

El grupo de las cloroquinas posee un efecto antireumático en algunos pacientes con artritis reumatoide. Es necesario tener una serie de experimentos mas controlados y mas prolongados para evaluar propiamente la actividad antireumática de estas drogas.

The Chemical Warfare Threat*

by

Colonel Victor C. Searle, U. S. Army†

Chemical agents, some of which are not detectable by human senses, can produce mortality and morbidity in large populations. Such materials can at present be produced in large amounts by any major power. Protective devices effective against some nerve gases will be produced commercially in 1961. Psychochemical drugs, capable of disrupting a military force without permanent damage, are being developed. Such temporarily disabling weapons would be most applicable in a non-nuclear war, especially a "limited" one. Means of early detection and treatment require urgent investigation; adequate defense necessitates nationwide knowledge of the available facts. SVH

MY purpose today is to present to you certain aspects of the present threat against the United States and its Allies which is associated with the possible use of chemical weapons in warfare. I propose to do this by summarizing for you in general terms the military capabilities and hazards with respect to chemical weapons now generally known to exist; I shall then give you some glimpses of what future developments may be like in this field, and the problems that may arise.

To begin with, let me define my terms. From the military point of view, the term "chemical weapons" includes not only the well-known "war gases" as they are commonly called, but also the use of flame and smoke on the battlefield. I shall confine myself entirely to the so-called "war gases". This term in itself is inaccurate, since many of the chemical compounds concerned are not gases but rather liquids or even solids under ordinary conditions. However, the term has the sanction of established usage; everyone knows what it means; it refers simply to the large-scale use of toxic chemical agents for their direct casualty-producing effect on the individual after they have come into contact with his skin or been absorbed into his body.

The use of chemicals in warfare for direct action on the body of the individual soldier is by no means new, going back literally for thousands of years. The modern use of chemical weapons on the battlefield was initiated in World War I by the Germans, when in April 1915 they loosed a cloud of chlorine gas against the Allies in France. As everyone knows, the effects of this gas attack were profound and demoralizing, but were not exploited in such a way as to effect significantly the outcome of the war, and very shortly after the initial attack, chemical warfare was raging with equal intensity on both sides of the battlefront.

An interesting aspect of the use of chemicals in World War I is the number and variety of different chemical compounds which were used or even considered. A partial list of these substances is shown in Table 1. In general, one may say that each side was attempting to surprise the other side with a new and more potent chemical for which existing defenses were inadequate. Note particularly that a number of promising

*Presented at the Medical-Health Section, Ninth United States Civil Defense Council, Minneapolis, Minnesota, 21 September 1960.

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chemical agents did not reach the stage of battlefield availability during World War I, largely because sufficient quantities had not been produced by the time the war ended.

Research on chemical warfare agents did not stop after World War I. Some of this research resulted in the discovery of vastly improved chemical warfare agents, particularly in Germany, as we shall see. Much of the research resulted in the elimination of all but a handful of chemicals as being of practical battlefield significance. At the time of World War II, for example, the only chemicals considered to be of practical significance to the United States and its Allies included the mustard gases (both ordinary or sulfur mustard and the newer nitrogen mustards) phosgene and related compounds, and, for specialized use, hydrocyanic acid.

However, the Germans had made a secret and startling advance in chemical warfare, not discovered until after World War II was over. This was the discovery by the German scientist, Schrader, of the "nerve gas" type of compound, in 1939, during a routine search for more effective insecticides.

The term "nerve gas" refers to a group of highly toxic chemical compounds, which are generally organic esters of substituted phosphoric acids. They are anticholinesterase agents closely related in their effects to commercial insecticides such as Parathion and Malathion.

The compound known as Tabun is the nerve gas which the Germans had available in quantity during the closing years of World War II. A large German plant for the manufacture of Tabun was captured by the Russians and has been moved back to Russia, where presumably it is in operation today.

The second of the two nerve gases shown, Sarin, which is known to us as "GB" was not available to the Germans in quantity during World War II. Much research on the nerve gases after the close of World War II led to the decision that Sarin was superior to Tabun for military purposes. It has been exhaustively investigated with respect to its possible effects on the battle field.

The nerve gases introduced several new elements into the war gas picture. The first of these was a significant increase in lethality over previously known chemical agents. This increase in lethality is at least one order of magnitude or more over that of previously known chemical agents. With such an increase in potency available, it became possible for the first time to consider seriously the dissemination of chemical agents in other than local tactical situations, i.e., delivery by aircraft or missiles at long range. Such long range delivery of toxic chemical weapons must now be considered to be a real threat, one which did not exist prior to the discovery of the nerve gases. Furthermore, this threat may well increase in intensity as even more potent chemical weapons are discovered, as they most surely will be with continued research in this field.

It is sobering to realize that any major military power can manufacture GB or a comparable material at the rate of hundreds of tons per day. GB is a liquid, but a volatile liquid. When disseminated as a military agent, it will usually appear in a vapor form – a true "gas". The major portal of entry is inhalation. It can also enter by contact with the eyes. Consequently, an effective mask offers essentially complete protection. So long, however, as the civilian population is not possessed of individual masks and the training to use them, GB poses a serious threat. A single large enemy missile could disperse enough GB to produce at least 30 per cent casualties among all unmasked personnel in the open over an area one mile in diameter. By "unmasked" I mean people who are not actually wearing their masks when the attack occurs but are carrying them or have them nearby. A one mile circle over a metropolitan target would encompass many thousands of people.

Now a new development has come along to confuse the picture. Anticholinesterase toxics of low volatility are available. When deposited on the skin these compounds do not evaporate and blow away (relatively harmlessly to a masked individual), but they penetrate effectively. They are highly toxic. The exposed skin of the back of the hand, or even a single ear lobe, is a sufficient portal of entry. The deposition may be made in the form of a tiny, but visible droplet,

which goes unnoticed, because it is quite painless, and symptomless except systemically. Or the deposition may be in the form of impaction of a subvisible, fog-like aerosol.

A second new element in the chemical warfare picture is due to the fact that the nerve gases are generally colorless, odorless or nearly so, and are readily absorbable through not only the lungs and eyes but also the skin and intestinal tract without producing any irritation or other sensation on the part of the exposed individual. Prior to the advent of the nerve gases, practically all chemical agents which might be expected on the battlefield were recognizable by a characteristic odor or irritation so that detection of exposure was possible almost simultaneously with the exposure itself, and protective measures could be instituted immediately.

With the nerve gases, the lack of ability of the human senses to detect their presence, and the possession of such potency so that even a brief exposure may be fatal, has created entirely new defense problems. It is clear that if we cannot detect these agents by our senses we must turn to the chemist and engineer for chemical and physical methods of detection; these detection measures must be available for large area coverage as well as for the use of the individual in a contaminated environment; they must be highly sensitive and specific, rapidly acting, and if possible automatic and continuous in operation. Paralleling the development of such warning devices must come an improved efficiency in individual protection, not only for the familiar respiratory protector or "gas masks", but also for the protection of the entire body area of the individual. At the same time we must recognize that even the most adequate warning and protective devices will not entirely prevent the production of nerve gas casualties, and a strong medical research program on prophylaxis for and therapy against poisoning from the nerve gases must be vigorously and successfully prosecuted if we are to minimize the threat from these new and extremely potent chemical weapons.

Let me digress for a moment to review the status of physical protective equipment for the civilian population. I should emphasize that the items I shall discuss furnish full protection against biological attack via the respiratory route as well as against chemical agents.

The OCDM organizational mask now known as the CDV-800, is very similar to the military mask. It is intended for civil defense workers who must continue to function and carry on outside activities during a BW or CW attack. OCDM and the State and local civil defense organizations have some 42,000 of these organizational masks in their supply system.

For the general population, the Chemical Corps has developed, under OCDM auspices, the civilian protective mask to be known as the CDV 805. The protection it affords is fully equal to that of the organizational mask but it is somewhat less rugged and less comfortable to wear under conditions of heavy physical exertion. It would be expected to withstand fewer attacks with a given agent than the larger mask which carries more charcoal.

The current OCDM budget for FY 1961 carries funds for production testing, and tooling-up for this mask. OCDM plans contemplate that it will be manufactured and distributed commercially for purchase by the individual. The price should be in the range of $2.50.

These masks come in six sizes which will fit all persons from four years old and up. For children younger than that an infant protector has been developed, also by the Chemical Corps. As you can see, this is similar to a small tent with plastic windows and panels of filter material. It is still under engineering test, and will become available somewhat later than the protective masks.

So much for individual protection. It is also possible and essential to protect individuals in groups, as in shelters. Filters and equipment have been developed for protecting large installations where power is available for ventilation. In effect, these filters simply constitute large scale protective masks for rooms or building spaces rather than for individual people. A unit consists of particulate filters to screen out BW particles and activated charcoal filters for removing chemical agents.

Present OCDM policy requires that all new Federal buildings have provisions for installing these filters as a later date and the same policy is recommended for State and local governmental agencies and industrial centers.

As I said, these depend upon continuing sources of power. At present there are no comparable units available for incorporation into the home fallout shelters which are being recommended. This problem is under study by OCDM, however, and it is hoped that before too long such units will be commercially available and adapted to hand-blower operation.

We cannot afford to ignore the real possibility that even more powerful chemical weapons than the nerve gases remain to be discovered. There are many toxic substances known today which are more lethal on a weight basis than any of the nerve gases. Some of these substances can be made in the laboratory. Others have been found in nature. Among the compounds which can be made in the laboratory, one of the more interesting is a complex aryl carbamate synthesized some years ago by French investigators(1).

This substance has a lethal dose in the mouse and in the rabbit which is only about 1/10 that required for the nerve gas, GB.

While it is doubtful that the compound in question will ever be of military significance for a number of reasons, among them being the complexity of the molecule and its difficulty of synthesis, the point is that the chemist knows about and can synthesize lethal chemical compounds which are far more potent than the nerve gases. There is no reason to expect that research will stop at this point; on the contrary, we should not blind ourselves to the real possiblity that the nerve gases will become as obsolete in the future as they have rendered obsolete many of the chemical agents of World War I and World War II.

I should now like turn my attention to a second type of chemical weapon, one which is rather new but which has already attracted considerable military interest throughout the world. I refer to the large-scale use on the battle field of chemicals which are not basically lethal in themselves but which produce a temporary and reversible incapacitation, as for example by producing temporary mental confusion, temporary anesthesia, narcosis, paralysis, temporary blindness. Such chemicals used in conjunction with other non-nuclear arms could contribute to the success of a military operation, with a significant reduction in loss of life — particularly in comparison to the casualties associated with nuclear use. An example of a situation where nonlethal weapons might be of considerable significance is found in so-called "limited" wars, or less than total wars, where military operations are limited in scale, area, participants and degree of violence. In such wars it is desirable to stamp out the aggression at the earliest possible moment and with minimum loss of life and property.

In these circumstances, the incapacitating agents might be a usable discriminating force which, in support of other non-nuclear weapons, could make the attainment of battlefield objectives much simpler for the nation employing them.

One might ask at this point whether or not chemical compounds exist which can produce temporary incapacitation to a degree which will be militarily significant, without a high lethality. Two examples will be cited. In its recent report entitled "Research in CBR (Chemical, Biological and Radiological Warfare)", the Committee on Science and Astronautics of the U. S. House of Representatives referred to demonstrations of drugs which incapacitate by both physical mechanisms and mental mechanisms. In this latter class, commonly referred to as "psychochemicals", reference was made to the well-known drug lysergic acid diethyl amide, or LSD 25, as it is more commonly known. This drug will be discussed shortly. The House report also cited a statement by Maj. General Drugov, of the Soviet Army, to the effect that "special interest attaches itself to the so-called psychic poisons (mescaline, methedrine, lysergic acid derivatives) which are now used for the simulation of mental disease."

Let us look at the chemical nature of some of these compounds. Mescaline, one of the compounds mentioned by General Drugov, is a compound of rather simple chemical structure, found naturally in mescal buttons, a portion of a small

cactus plant used as a stimulant and mild intoxicant, particularly by Mexican Indians in certain ceremonials.

The pure material produces in man a profound hallucinatory condition at dose levels of approximately 30-50 milligrams per man. However, the relation between chemical structure and psychochemical activity is not at all understood as yet, and there is no reason to believe that further research on the relatively simple mescaline molecule may not yield compounds into the same pharmacological action which are more potent on a dosage basis than is mescaline itself. If such more potent compounds are found, they may well prove to have practical military significance.

Among the lysergic acid derivates, also mentioned by General Drugov, lysergic acid diethylamide or LSD 25, has attracted considerable attention, particularly in the field of experimental psychiatry. This substance is a synthetic compound first made by Stoll & Hofmann(2) almost 20 years ago. The synthetic process consisted in the preparation of the diethylamide derivative of the naturally occurring lysergic acid, which latter is obtainable from ergot. LSD 25 is an outstanding example of a psychochemical drug, i.e., one which exerts its action entirely or almost entirely on mental processes. In very small doses, of the order of 1/20th to 1/3rd of a milligram, the drug produces in man such an extreme degree of mental confusion that the individual is for all practical purposes incapable of carrying out his normal duties. The effects may last for a number of hours, depending largely upon the dose given, and then wear off completely, leaving no discernible after-effects. The lethal dose of LSD 25 in man is not known, but on the basis of animal experiments it is estimated to be from 100 to 1000 times as high as the biologically effective dose.

You will have noticed that the compounds cited as examples of incapacitating, essentially non-lethal, chemical compounds which might be of military significance are all characterized predominately by action on mental processes. There are many other mechanisms which may be exploited as the basis for incapacitation on the battlefield. Some of the more obvious mechanisms include temporary paralysis, either partial or total; controllable narcosis or sleep-inducement; reversible and temporary elimination of the sight, the hearing, or the sense of balance; persistent lachrymation, diarrhea, or vomiting; temporary convulsive spells; and other mechanisms will no doubt suggest themselves. We must be aware of the fact that drugs are known at the present time which can produce any of the effects cited, frequently at a very low dosage. The existence of these drugs is by no means a guarantee that they have battlefield potentiality, but it may not be too difficult a step to convert known drugs into military weapons by the use of an intensive research and development program directed towards this end. It should be recognized that the deliberate search for chemical weapons of the type I am describing is relatively recent, and has not in the past been one of the primary objectives of either the drug industry or of military research laboratories. Now that the possible significance of weapons of this kind is realized, it is almost impossible to predict what may appear in the future, but it should be clear to all that many new and interesting developments may well be expected in this field.

We cannot afford to ignore the problems which may be posed by the military use of non-lethal incapacitating chemical weapons, either overtly or covertly. The wide variety of drugs which influence either the mind of man or his body represent an ever increasing challenge to our ability to discover such drugs, to determine how they act, and to erect defenses against them.

In summary, then, this is the CW threat. The more potent chemical weapons of previous wars are still available, with established manufacturing and delivery capabilities on the part of any large nation which chooses to use such weapons. In addition, there are the newer and far more powerful nerve gases, likewise associated with established manufacturing and delivery capabilities. The lack of ability to detect the presence of nerve gases by the senses, and their high potency and speed of action, stresses more strongly than ever before the need for suitable means for detecting these agents, for protection against their effects, and for the treatment of casualties therefrom should these occur. Furthermore there is no reason to believe that the limit of

potency in lethal chemical weapons has been reached in the nerve gases, and a continuous research program, looking well beyond the potency limits of the nerve gases, is essential if we are to keep up with the scientific and technological progress which will undoubtedly occur in this field, as it does in all other areas of science and technology.

Furthermore, we have considered briefly a relatively novel concept of chemical compounds in warfare, namely the use of incapacitating nonlethal drugs, which may affect either the mind or the body of exposed personnel in such a way as to contribute significantly to military success for the nation employing such compounds on the battlefield.

I have indicated to you that the defensive problems are formidable, and urgent. To meet the CW threat, it is imperative that all elements of our population be aware of the existence and magnitude of this threat, and be alert and responsive to the provision of means for defense against this threat. Such means include an active civil defense organization, readily available means for use in defense against chemical agents, and support of a vigorous research and development program on chemical agents to provide for the continuing awareness of new elements of danger in this important weapons area, thus to be better prepared than we are now for the use of chemical weapons against us.

TABLE 1
PARTIAL LIST OF DIFFERENT CHEMICAL COMPOUNDS WHICH WERE USED OR CONSIDERED IN WORLD WAR I

TEAR GASES
Ethyl bromoacetate
Chloroacetone
Xylyl bromide
Benzyl bromide
Bromomethyl ethyl ketone
Bromoacetone
Iodoacetone
Ethyl iodoacetate
Benzyl iodide
Acrolein
Bromobenzyl cyanide
Chloroacetophenone

CHOKING GASES
Chlorine
Methylsulfuryl chloride
Chloromethyl chloroformate
Ethylsulfuryl chloride
Dimethyl sulfate
Perchloromethylmercaptan
Phosgene
Perchloromethylmercaptan
Phosgene
Trichloromethyl chloroformate (diphosgene)
Chloropicrin
Phenylcarbylamine chloride
Phenyldichloroarsine
Dichloromethyl ether
Ethyldichloroarsine
Phenyldibromoarsine
Dibromomethyl ether

BLOOD POISONS
Hydrocyanic acid
Cyanogen bromide
Cyanogen chloride

BLISTER AGENTS
Dichlorethyl sulfide (mustard gas)
Chlorovinyldichloroarsine (Lewisite)
Methyldichloroarsine
Dibromoethyl sulfide

VOMITING GASES
Diphenylchlororarsine
Diphenylcyanorarsine
Ethylcarbazol
Phenarsazine chloride (Adamsite)

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Ambroise Paré

Surgeon of the Renaissance†

Paul J. Matte, M.D.
Phoenix, Arizona

IN ABBREVIATED and superficial works on the history of medicine are found such statements as these: "Ambroise Paré was the greatest surgeon of the Renaissance," or, "Paré is the Father of Modern Surgery"; and both of these he was, but the manner in which he became so is worth a moment's consideration. For, as the Renaissance itself did not burst fullbloom upon the stage of history, neither did Paré singlehandedly effect a renaissance of surgery. He was born in 1510, when the Renaissance had already been in progress a respectable period of time. And he stood upon the shoulders of his immediate predecessors to attain the eminence which was later his. His innovations were few in number, and those advancements usually attributed to him were anticipated, and indeed, even published, by others who went before him. Of his manual skill in surgery we know little . . . in his writings he seems at times almost to depreciate this attribute of the surgeon, saying: "I had my servant do this," or "in order to give him experience, I had my apprentice do that." He invented no instruments*, using those which came to his hand from the armamentarium of the surgeons of the time. By the standards of his day he was ignorant, knowing nothing of Greek, and little of Latin. He was perhaps the most unlikely of men to have attained the greatness which was later his. And yet, with all these negative attributes, he *was* the greatest surgeon of the Renaissance period, and he *was* and *is*, the father of modern surgery.

Let us see, then, how this came about. Someone has said that it is not men who make the times, but the times which make the man, and, as we shall see, the world, and particularly the world of medicine, was waiting and ready for Paré, when he came upon the stage.

He was born, as has been said, in 1510, and his contempories, if not his associates, were names of undisputed greatness. Leonardo, Michaelangelo, Vesalius, Montaigne, Rabelais, Luther, Calvin, and others of equal stature. It is believed that he knew Vesalius, and to him and to Leonardo, owed much of his knowledge of anatomy. He was caught in an intellectual, an artistic, and an anatomical stream of a power which the world has not known before or since; the world was ready for Paré and his work, and it is to his everlasting glory that he did not let the chance go by.

He was born in France, in the city of Laval, of a family which we would now consider middle or lower middle class. His father was a barber and *valet de chambre** to a member of the lesser nobility, and his brother-in-law was a barber surgeon, practicing in Paris. Although the details are not available, Paré is believed to have begun his medical career by working with a

*He developed but did not invent an obstetrical forceps, with four hooked blades on the fetal end, of rather horrendous appearance.

†Read before the Phoenix Society for the History of Medicine, Sept. 30, 1960.

*Singer (1) states Pare's father to have been a boxmaker. I have been unable to reconcile this conflict of authorities.

provincial barber surgeon, until he entered an apprenticeship to a barber surgeon in Paris in 1533, when he would have been twenty-three years old. He was thus, at this time, almost as low in the medical heirarchy as it was possible to be.

For the medical profession in France in the 16th century was organized into several classes, mutually antagonistic. There were, at the very bottom of the pyramid, itinerant and irregular practitioners, more or less adept at certain manual procedures, such as the lithotomists, the sowgelders, and the bonesetters, coequal with the midwives and *sage femmes* of the day. Next above these came the barber surgeons, who had the advantage of a guild, certain standards, and a tradition of manual competence. Their social status was roughly that of tradesmen or journeymen. In an interesting parallel to our own day, the barrier which separated these lower groups from the higher was that of a University education, represented essentially by a knowledge of Latin and Greek. It was this lack, of which Paré was himself acutely aware, as his writings abundantly show, that was responsible for most of his later difficulties with the organized medicine of his time, and which was indirectly, a major factor in his later greatness. For, as Paré himself points out in his *Apologie and Treatise*(2), the reason for his ignorance of classical languages was that he was much too busy in his youth learning surgery the hard way; and it was his lack of Latin which forced him to write of his discoveries and controversies in the vernacular, and led to the great reputation which was his in his own lifetime.

Someone has said, in this connection, that had Paré known Latin he would never have written his treatise on obstetrics, or, had he written it in Latin, none of those for whom it was intended would have been able to read it, since obstetrics was in those days in the hands of the midwives, mostly, and the barber surgeons occasionally.

In any event, we find Paré, at the age of twenty-three, at work in the lower ranks of Renaissance medicine — at this time actually medieval medicine — devoid of a college education, and apparently forever doomed to mediocrity.

Next above him we find the Surgeons of the College of Saint Come, the surgeons of the long robe, as the barber surgeons were the surgeons of the short robe. These Surgeons of the College were University graduates, and knew their Latin and Greek, and in a fashion reminiscent of our own, were continually engaged in intellectual and political controversy with the physician members of the Faculty of Medicine of the Sorbonne, who looked down upon them as their social and intellectual inferiors. The Surgeons of the College limited themselves to superficial applications and manipulations, and to minor surgery, all wrapped in much medieval theory and quoting of Aristotle, Galen and other ancient authorities. Unfortunately, though they knew their Latin, they knew little of actual surgery, considering such messy, pragmatic matters as amputations as beneath their position. It is difficult from our viewpoint to see that they served any function at all, and this seems to have been Paré's attitude in his early writings. And we begin here to see shaping that battle which was to occupy Paré, between wars, for the rest of his life.

For reasons which probably had to do with his innate talents, Paré did not remain long an apprentice. About 1534 he was appointed a resident surgeon in the Hotel-Dieu, the only public charity hospital in Paris. This was an appointment much sought after, and his selection for the post seems to have been the first professional recognition of Paré's inherent ability. He remained about three years, and as surgeons of today speak for the rest of their lives of their days as house officers, Paré in his writings refers frequently to the experience gained in what was in effect his residency.* It is believed that he left the Hotel-Dieu qualified for but financially unable to open a practice, probably because he could not raise the necessary license fee. It is, at this point, and by the fortunate circumstance of his poverty, that Paré first comes upon the scene of medical history.

Reference to any history of the Sixteenth Cen-

*One of Pare's few faults seems to have been a reluctance to give credit where credit is due There is in his works no specific mention of his teachers at the Hotel-Dieu, although their names are known from other sources. And it was not until later editions that he credited his fellow barber surgeon de Heiry with co-authorship of the work on anatomy.

tury will show this period to have been one of continuous religio-political wars, as adherents and claimants to the French, Spanish and Italian thrones fought for the control of Europe, in the political chaos resulting from the collapse of the Holy Roman Empire.

It was the custom at that time for the leader of an army, most commonly a member of the nobility, to provide himself with a surgeon or surgeons, primarily for his own protection and only secondarily for the care of his men. Much of Paré's early reputation derived from the fact that he, a surgeon to the officers, should trouble himself with the care of the wounded common soldier. Space does not permit a digression into the history of warfare, but it should be noted that armed combat in the Sixteenth Century afforded more brutal and intimate contact between the participants in a battle, in association with the close-up use of primitive firearms, than history has offered before or since, with the possible exception of our own Civil War.

For these Sixteenth Century warriors were caught in the transition from chain mail, personal armor, pikes, lances, halberds, and maces, to the use of firearms, with the burns, concussion and miscellaneous trauma of primitive bombards, harquebuses, and cannon, using unstable and primitive gunpowder in a combination equally dangerous to friend and foe. The result was a variety and severity of wounds unequalled in the history of medicine until the advent of the modern motor vehicle.

Paré's case reports can give a modern surgeon pause, as he describes such problems of burns complicated by pieces of mail driven into the wound by the primitive weapons of the day.

It is an adage older than Paré that the battleground is the true school of the surgeon; and it is a circumstance unique in the history of medicine that Paré was for almost forty years continuously engaged as a military surgeon, in attendance upon the French kings and commanders of the period.

And so Paré's fame rests like a stool, upon three legs, two of which we have already seen: he was born at the right time and in the right place and was spared the intellectual stagnation of a classical education; he was afforded the opportunity of a surgical experience such as no surgeon has had before or since; and lastly, he wrote of his experience and the lessons he had learned. For, had Paré not been a writer, and a competent one, and had he not written in the vernacular, we should know little of him today, and his influence would have been less, and surgery the poorer. But write Paré did, prolifically, pragmatically and polemically, over a period of forty years.

It was following his second campaign, and most probably at the instigation of Sylvius, of cerebral aquaduct fame*, that Paré wrote and published his first book. The title bears repeating, for it sets the tone of all his later works: *"The Method of Treating Wounds Made by Harquebuses and Other Firearms: and of Those Which Are Made by Arrows, Darts, and Similar: Also of Burns Made Specially by Gunpowder."*(3) In 1549, between wars, he published a treatise on Anatomy and Osteology, after one or two years of intensive study of the subject, in which he worked with a fellow barber surgeon to dissect the whole of one side of the body of a criminal. He later claimed to have kept the body and its organs preserved for study and in good condition for twenty-seven years. This anatomical treatise is noteworthy for an appendix which contains accurate and adequate instruction for the obstetric operation of Podalic Version, for which Paré claims no originality, but which he is usually credited with bringing into use.(9)**

His next publications were in 1561, several wars later, although he had obviously been working on them for some time. These were: *"The Method of Curing Wounds and Fractures of the Human Head,"* and *"Universal Anatomy of the Human Body."* Three years later, following the sieges of Bourges and Rouen, he published his most important work, so far as the furtherance of practical surgery was concerned, the *"Ten Books of Surgery, With the Kit of Instruments Necessary to It."* This was a veritable course in surgery, the first volume containing the general attributes of the surgeon, and the basic principles of the art. Others deal again

*As might be expected, Sylvius did not discover this structure. He merely described it louder than anyone else. His most striking claim to fame is as the teacher of Vesalius(4).

**A few years after his death, Pare's daughter was seen successfully through a difficult delivery by one of Pare's pupils who stated that the successful outcome was due to Pare having supervised him in the management of a similar case years before.

with gunshot wounds, and with the use of the ligature in amputations, another innovation — actually a rediscovery, which is usually credited to Paré. The book was written in the vernacular, and when Paré was criticized for having done so, and efforts were made to suppress it, he again pointed out, quite reasonably, that he had written it for the education of young surgeons, and that if it were in Latin those for whom it was written would be unable to read it. Other books followed, but it was the publication of the *Dix Livres* which led to the controversy which was to occupy Paré for the remainder of his professional life. It had been simmering for several years, and now came to a boil.

As a result of his early campaigns, and his successful treatment of war-injured noblemen, Paré had come by 1554 to occupy the position of court surgeon. Just which and what court is at times a bit difficult to say because of the complex political intrigues of the day, but his principal patron for many years was Henry of Navarre, afterwards King Henry IV of France. In this capacity he was continually on loan to various lesser monarchs of France, depending on who was doing the fighting at the time. Some insight into his remarkable personality is found in the fact that he at times functioned as a diplomatic emissary for his patrons. The most interesting of his accounts of these political activities is found in his report of the Siege of Metz, found in his *"Treatise and Apologie."*(3)

By 1554 his prestige and reputation were such that the surgeons of the College of St. Come, in essence the Royal College of Surgeons, felt the necessity of having him as a member. In this the surgeons of the College appear to have been motivated less by an admiration for Pare than by the necessity for reinforcements in their battles with the Faculty Physicians above them and the Guild of Barber Surgeons below them. (1) And so, in spite of his deficiency in classical languages, Paré was passed through the formalities of initiation without examination, and without the usual fees. What Paré thought about all of this is not exactly known, but it is certain that the change from the short to the long gown of the university surgeon did not alter him in any particular way.

From what we can deduce of Paré's character, the entrance of this pragmatic and superlatively competent surgeon into the rarefied and scholastic atmosphere of the College of Surgeons of the Sorbonne could have produced nothing but conflict, and so it did, for the next ten years. He was attacked and vilified by various members of the Faculty of Medicine as an ignorant charlatan, and in 1572, published his *Five Books of Surgery*,* dealing chiefly with fractures and dislocations and answering the virulent attack of one Julien de Paulmier, who, in a book written in 1569, had questioned Paré's treatment of gunshot wounds. Various books followed, dealing with monsters, plague, and surgical procedures.(1) And in 1575, following the publication of his collected works, Paré was in effect sued for malpractice, by being hauled up before the ethical committee of his society on the charge of writing in the vernacular and publishing without the approval of the Faculty, under an old ordinance. This charge was pressed by one Gourmelen, a physician of the Medical Faculty of the Sorbonne, and it is a sad commentary on human nature that it was supported by a majority of Paré's colleagues of the College of St. Come. Although Paré was found guilty, no action was taken, and his book was not suppressed.** He continued to function as medical attendant to the King under the title "First Surgeon of the King," and in the third edition of his works in 1585, published his *Apologie and Treatise* which is a reply to his accuser, in the form of a debate, and contains the biographical record of his experiences in the wars from which he acquired his vast knowledge.

It was in connection with his activities in medical politics that Paré suffered his only personal defeat. In 1567, by virtue of his membership in the College of St. Come and his position as First Surgeon of the King, he tried to bring all those who practiced surgery in France under his control, instead of under that of the Premier Barber Surgeon. This aroused great opposition, and he was forced to abandon the effort.

Most of what we know of Paré the man is gleaned from his last work, the *Apologie and Treatise*. It was written in 1585, when Paré, no

*The bibliomaniac will be interested to know that there is no known copy of this **Cinq Livres** in existence.

**There was some justification to this charge. As he gained in experience and prestige, Pare had begun to write on purely medical matters. In the highly-specialized 16th Century, this was bad manners if nothing else. (1) (3)

longer actively engaged as a military surgeon, was nearing the end of his life. It is a remarkable work, containing as much of politics and history as of surgery. It has been described as "the most entertaining surgical treatise ever written," and is in truth a difficult book to put down. Paré wrote his apology in answer to the charges of malpractice leveled against him by the Faculty of Physicians, in the person of Étienne Gourmelen. In the book, Paré undertakes first to demolish his opponent, and second to prove his own merit by a recital of his experiences and successes. It is a work necessarily egoistic, as any autobiography must be, but there is nothing false about it, and between the lines comes to life the figure of a man of intense practicality and profound common sense; of vast experience and the obvious ability to learn from it. The case histories of traumatic injury are superlative in detail and diagnostic acumen. There is little difficulty in making a diagnosis in modern terms from the information supplied by Paré. With respect to clinical detail and prognostic acumen he must be admitted the superior of Hippocrates, who is sometimes maddeningly vague.(7)

Those familiar with the works of both Hippocrates and Paré cannot but be struck by the similarity of the two men in approach and mode of thought. It is also apparent that we have in the two of them the archetype of the physician and of the truly great surgeon. Hippocrates observes, asks questions, makes deductions of a general nature, prognosticates, and as often as not, does nothing to alter the course of the disease. Paré, confronted with a surgical problem, draws upon his experience, reaches a conclusion as to the probable outcome of the situation, and proceeds to apply pragmatic remedies. In contrast to Hippocrates, he is not unwilling to undertake the losing battle, (cf. his clinical record of the severe chest injury of one Lord Martigues*). There are, however, points in common between the two. Each had little patience with unproved theory, or that which did not accord with the facts. But whereas Hippocrates seems happiest when dealing with generalities, and in formulating his own theories, Paré is at his best with the individual case, and with his hands in the gore. To Hippocrates and his school is usually attributed the invention of clinical observation as the foundation of medical science, and the deduction of principles therefrom. If the Renaissance was in truth a rebirth of the scientific approach and the rediscovery of ancient principles, then Paré is the only and logical successor to Hippocrates. Not excepting Galen, there is no one in between.

Some idea of the force of Paré's influence upon modern surgery can be gained by a comparison of his techniques with those in use in the pre-aseptic era of the late 19th Century. In the French school particularly, the similarities are startling.(5)

No introduction to Paré can be complete without quoting the experience of his rst campaign, in which, characteristically, he made his first important discovery. The excerpt serves also to give the stranger to his writings the flavor of Paré. (Voyage of Turin, 1537)(8) (2).

> " . . . Now at that time I was a fresh water souldier, I had not yet seene wounds made by gun-shot at the first dressing. It is true, I had read in *John de Vigo*, in the first booke of wounds in generall, the eighth chapter, that wounds made by weapons of fire did participate of Venenosity, by reason of the pouder, and for their cure commands to cauterize them with oyle of Elders scalding hot, in which should be mingled a little Treackle; and not to faile, before I would apply of the sayd oyle, knowing that such a thing might bring to the Patient great paine, I was willing to know first, before I applyed it, how the other Chirurgions did for the first dressing which was to apply the sayd oyle the hottest that was possible into the wounds, with tents and setons; insomuch that I tooke courage to doe as they did. At last I wanted oyle, and was constrained in steed thereof, to apply a digestive of yolkes of egges, oyle of Roses, and Turpentine. In the night I could not sleep in quite, fearing some default in not cauterizing, that I should finde those to whom I had not used the burning oyle dead impoysoned; which made me rise very early to visit them, where beyond my expectation I found those to whom I had applyed my degestive medicine, to feele little paine, and their wounds without inflammation or tumor, having rested reasonable well in the night: the other

*Voyage of Hesdin, 1553. (1) (3) (9)

to whom was used the sayd burning oyle I found them feverish, with great paine and tumour about the edges of their wounds. And then I resolved with my selfe never so cruelly, to burne poore men wounded with gunshot."

There has been much speculation of Paré's philosophy, and of his religion. It is characteristic of Paré that for all his involvement in the religio-political intrigues of the time (someone has referred to his ability to keep his footing on the slippery ground of Renaissance courts), that it is not known definitely to this day whether he was a Protestant or a Catholic. It is generally believed that he followed the outward forms of Catholicism as the occasion required, but was by conviction probably a Protestant.(1) One of the legends of Paré has it, apparently with accuracy, that his last patron, Charles IX, a Catholic, protected Paré from those who sought to destroy him as a Protestant, and went so far as to save his life during the Saint Bartholomew's Night massacre of 1572, by hiding him in the royal bedchamber.(6)

Although many attempts were made on his life, and he was often in danger during his many campaigns, Paré seems to have led a charmed life, and relates only two incidents of significant trauma. He was once given poison,(9) but discovered it in time to apply an emetic and antidote; and he sustained, ironically between campaigns, a compound fracture of the leg from the kick of a horse. This last episode is of particular interest inasmuch as the usual treatment for such injuries, as late as our own Civil War, was amputation. The details of his treatment are, alas, lacking, but Paré demonstrates the typical surgeon's interest in the integrity of his own person, and recovered without less of the extremity.

It is pleasant to relate that Paré attained in his lifetime rewards commensurate with his ability, and lived to retire a comfortably wealthy man. He emerged from his retirement in the last year of his life to intercede with the Archbishop of Lyons to end the suffering of the populace of Paris by surrendering to the city's besiegers, a plea which was granted.

He died in 1590, and was buried in the Church of St. Andre des Arts. His statue in Paris contains the essential philosophy of Paré, in an inscription familiar to every medical schoolboy:

Je le Pansay, Dieu le Guerit
or
I dressed his wounds and God healed him.

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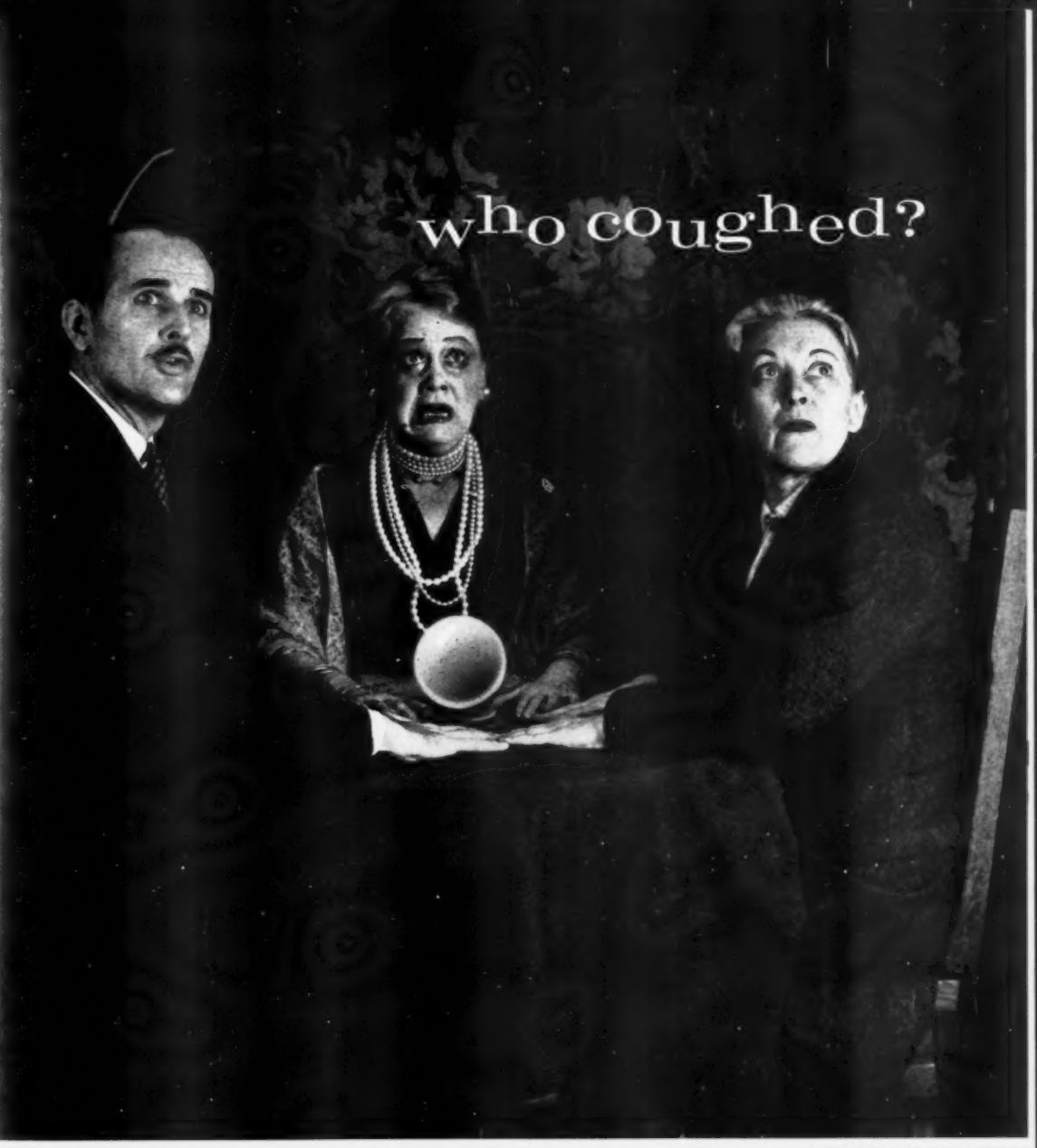

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The President's Page

The Education Of Politicians

Lindsay E. Beaton, M.D.

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There may be no more dangerous fact in the Twentieth Century than the fundamental ignorance of science of men who are charged with the responsibility of governments. The archaeologists of the future who try to puzzle out the reasons for the dissolution of Western Civilization may well conclude that it collapsed because it did not make use of the scientific and technical knowledge available to it. This is not an eccentric personal hyperbole; it is the considered opinion of the American Association for the Advancement of Science, the voice of the great majority of the country's scientists. The AAAS Interim Committee on the Social Aspects of Science four years ago noted that, "There is no impending crisis in the relationships between science and American society. This crisis is being generated by a basic disparity. At a time when decisive economic, political, and social processes have become profoundly dependent on science, the discipline has failed to attain its appropriate place in the management of public affairs." Updating the earlier report, in a recent statement in *Science* by the AAAS Committee on Science in the Promotion of Human Welfare it is decided that, "In the last few years the disparity between scientific progress and the resolution of the social issues which it has evoked has become even greater. What was once merely a minor gap now threatens to become a major discontinuity which may disrupt the history of man." What is true of science as a whole is also true of one of its principal divisions, medicine. There is an equal ignorance of medicine by public men, an equal failure of medicine to attain a substantial role in the management of American society, and a widening gap between medical learning and its use by the directors of the political state.

No responsible observer will deny that our culture depends not only for its coloring but for its very existence on the disclosures of science and the applications of technology. Even those who deplore the actuality admit it with varying degrees of bitterness. We find ourselves in the midst of a social mutation that dwarfs the industrial revolution and is comparable only to such momentous landmarks on man's pathway as his descent from the trees or his discovery of agriculture.

In view of these realities it is startling and alarming that there is not only illiteracy about but also vast prejudice against science. Evidences and explanations are not needed in this place. Probably such anti-scientism is a form of general anti-intellectualism. In the health field this benighted bias is particularly virulent and particularly fearful. One needs only to call attention to the acceptance of such absurdities as Wilhelm Reich's orgone box, once believed in by as eminent an intellectual as Arthur Koestler, Hubbard's dianetics, various cancer cures, honey and vinegar for arthritis, or the strange and wonderful nonsense of chiropractic and naturopathy.

The politician becomes a special case in point. He presents this particular problem for scientific indoctrination because his position of lead-

ership in either the executive or the legislative branch of government makes him the contriver of the regulations under which the citizens will live. If the politician has no acquaintance with the principles of science, what it is, what it can do, and what it forecasts, he cannot very farsightedly conduct the frighteningly unstable course of a scientific and technical age. Little argument is needed to prove the deplorable misunderstanding of the politician about science. Our public men are largely attorneys and business executives; it is not surprising that they have little sensitivity to scientific thinking. An isolated example is hardly fair, but as an illustration let me cite the lack of understanding shown in a remark that the Republican candidate made during the recent Presidential campaign. He was attempting to demonstrate his grasp of the import of fundamental research as opposed to mere commercial inventiveness. He expatiated at length on the values of basic science only to end the entire speech with the observation that after all if dedicated laboratory men had not accomplished their wonders the world would not have the television on which the Vice President was being watched.

A few words on the problems that other sciences have with the politicians may remove from physicians any sense of neurotic uniqueness and may throw some light on the character of the difficulties and may suggest solutions. Paul B. Sears, certainly one of America's first-rate minds, remarked in 1956 of the question here being discussed, "I see little prospect of permanent relief unless we can establish among the American public and its political leaders a higher standard of scientific literacy than now obtains. I do not refer necessarily to the knowledge of the more esoteric and difficult aspects of science but to such very simple matters as the conviction that two and two make four, that water runs downhill, and that two bodies cannot occupy the same space at the same time."

The physicists and geneticists first of all have had a frustrating fifteen years, trying to persuade the powers that be of the tremendous catastrophe of repeated nuclear explosions in time of war and of the suicidal risk to the human race of radioactive fall-out. It has been difficult to convince either the public or its leadership just because neither is literate about the greatest danger ever to confront the species. The Federation of American Scientists resolved to publish its own non-technical magazine, *The Bulletin of the Atomic Scientists* with the prophetic clock on its cover, to attempt desperately to reach the intelligent public with information about the actualities of the era. The ecologists and other biologists have felt equally feverish in raising to popular attention the threat of population explosion and the consequent rapid exhaustion of the globe's natural resources. Some of them are openly pessimistic about the possibility of man adjusting his bionomic ways in time to avoid his final extinction on earth through the action of these natural forces. Changes have been induced in the physical environment that may eventually make mankind's existence untenable. Yet there is little evidence that the experts in the field have access to the politicians, or even that the latter know they exist. Our governmental leaders seem more prone to listen to the "practical men" who find in the proliferation of the populace a welcome addition to the industrial market and who blithely believe that the depleted mineral reserves of this rich continent will be magically replaced in the future. The biologists see the balance of nature tragically disturbed. They look on man as an animal who must live in harmony with his environment, and they see no confirmation of any such awareness on the part of the people who are trusted with the guidance of the great nations of the race. The chemists point to heedless pollution of our surroundings by the waste products of our industrial processes. Water and air contamination are a scandal, but the politician, no more than the public, gives any sign that he knows what the chemist is talking about.

What should be the scientist's role in public affairs? – be he medical scientist, physical scientist, biological scientist, or social scientist. One may conceive of three ascending steps of political involvement for him. He may first announce from his ivory laboratory that objectivity forbids any participation in social decisions beyond the provision of such data as he can accumulate. This point of view insists that the determination of values must be left to the general public, which assumedly has some special intuition in such matters, and that the scientist has no business using his prestige in behalf of a particular preference, and in fact

that he has no specific competence for such determination. A second and less aloof approach claims that the scientist must make available not only the facts as accurately as he can ascertain them and the hypotheses he derives from them but also must spell out very explicitly what he believes would be the results of various alternative courses. Tacit in such an analysis is a recommendation of a preferred line of action. If one choice will result in death and disease while another will result in longer life and greater health, it would seem obvious to the medical man that the latter would be preferred by all people. There is, finally, the third step, and it is this that the Federation of American Scientists felt itself obliged to take. This is the courage of commitment, espousing a cause and working for it. This is the action finally taken by natural scientists who feel that the plight of the world is close to hopeless unless men of good will exert themselves to implement what is to them rationally obvious. This is the judgment of men who find nothing in our past experience and nothing in the evolutionary process that can enable man to adjust automatically to the facts of the atomic age fast enough to ensure his survival past this century. This is the judgment that says that only through the exercise of man's intelligence and the farthest reach of his creative imagination can he perhaps ensure his biological inheritance. There are risks in the partisan method. There is the possibility that the scientist may lose his effective impact on public opinion by exhortation too frequent and too shrill. There is the hazard also of loss of his reputation for impartiality. In the face of the kind of jeopardy to the world represented over-population, war, radioactive fall-out and the exhaustion of natural resources, these objections lose their strength. Objectivity and scientific detachment are virtues. Survival is a virtue too.

The role of the doctor as medical scientist in the public arena is a little easier than the tasks of his brothers, the natural, social and biological scientists. It is easier because the doctor is committed without argument to a value judgment, that health is better than disease and that life is better than death. He is dedicated to a social purpose that almost every man will accept, the existence of the individual members of the species and the perpetuity of the race. He always stands for eagerly accepted propositions that enhance health and postpone death. The philosopher may depreciate the physician as a simple man. He is a simple man, impatient of debate about the worth of human life. Society would not have him other. It requires that the doctor be devoted to the concerns of health; it wants neither a nihilist nor a nonpartisan. The physician therefore is expected not only to declare the medical facts as he sees them, not only to clarify the alternatives for public decision in the field of health, but also staunchly to recommend a line of attack. The public-minded doctor often labors actively in behalf of measures he thinks necessary to implement his professional advice. He is not only the advisor of the citizenry about health, but he becomes the most spirited worker in the vineyard.

If politicians do not understand the broad connotations of scientific knowledge and method, no better do they appreciate the determining subtleties of health and disease. The legislator or government executive is usually concerned with a legal and economic picture of society and more recently with one that includes certain social aspects. Not as yet does he identify the historical forces and events that influence physical and mental well-being. In this area the doctor must educate the man of affairs. Only the legislator can minimize statutory lag. Only he can bring up to date the various health laws, can regulate business so that industrial practices do not produce illness, can rule that the freedom of the land is not to be twisted into freedom to cause disease, can overcome with law the illusory protection of the ancient warning of *caveat emptor*. But to accomplish these ends, he needs first to know the medical facts.

There should be both general and concrete items in the politician's medical education. It is not too much first of all to ask that he have a grasp of modern theories of disease. He should have acquaintance with the concept that disease is an adaptation to stress, so that he can conceive what the physical and psychological urgencies of modern life may mean to health. He should have some understanding of infection, of new growth, of degenerative processes, and of modern hypotheses of mental disease.

A few examples of specific health issues on which the politician needs indoctrination should serve to outline the ground. He should for ex-

ample know the possibilities of safe automobile construction, which might lead him to set legal standards to force the tycoons of Detroit to provide cars that are not merely stylish Juggernauts. The lawmaker should be shocked into action by the elementary recognition that traumatic injury ranks third among all causes of death in the United States and that more than half of all traumatic fatalities are related to automobile accidents.

Politicians should have brought clearly home to them the menace to health of water and air pollution. How many know the story of the five-day sulphurous smog of Donora, Pennsylvania, which in 1948 smote almost six thousand people and killed 18? Or are aware of the threats of industrial fumes in the environments of almost all major American cities? Or have even heard of the yearly epidemics of respiratory distress that strike the inhabitants of New Orleans, which have been related to certain air-borne wastes? How many realize that our waters have been so dirtied that beaches in the Great Lakes and even along certain coasts have had to be closed, or that in some towns tapwater foams like beer because of the detergents that befoul it? How many appreciate the sinister exposure to harmful chemicals in foods, or the possibility of causing deficiency diseases due to modern agricultural and food preservation practices, or the risks of estrogenic substances used in animal fattening?

There are other concrete health problems about which lawgivers need to learn, situations which only they can correct. For instance, the public is put in genuine physical jeopardy by the use of fluoroscopes for shoe fitting in department stores and shoe stores. Even in the enlightened State of Arizona it has not yet been possible to enact a pure milk law to avoid milk-borne disease. Fluoridation of public water supplies to prevent dental caries is strenuously opposed by a certain lunatic fringe of the public and needs official governmental backing. The danger of radioactive fall-out and of excessive radiological exposure from other sources cries for legislative acknowledgment and reduction.

Other areas in which the politician needs medical education are less immediate and evident. One can, however, hope that some day the legislator can be brought to know enough about genetic diseases so that laws may be passed to prevent their spread. A very striking recent example shows that such action is not infeasible. The administration of the Territory of New Guinea has announced a eugenic quarantine of the entire tribe of Fore, some thirty thousand people who inhabit almost a thousand square miles in the Eastern highlands of that island. Almost half the women and about a tenth of the men of the Fore tribe die of a hereditary neurological disease known as Kuru. This affliction is transmitted by a gene which is a Mendelian dominant in females and a recessive in males. Males therefore tend to move from the Fore region into neighboring tribal districts, carrying the lethal gene with them. To counteract this peril the government has prohibited emigration from the Fore area. Can anyone believe that our government, faced with a similar crisis in this country, would be able to impose an equally severe restriction to safeguard the public health?

Such a case leads one to the thought that the politician needs to be educated less to legislate with regard to explicit isolated health questions than to learn enough to provide the statutory authorization necessary to make modern scientific medical knowledge maximally available and operative. For example, the public man should command detailed comprehension of the practical workings and conditions of medical practice and how they are related to the care of the sick. It does no good to legislate against an organization of medical practice that has been determined to be the one that best provides for the health of the public, merely because the system does not suit a certain party line. Statutes are needed to eradicate such quackery as faith-healing, naturopathy, and chiropractic, and the politician must have familiarity with the fraudulence of such charlatans in order that he may be armed against the onslaught of those who scream that curtailment of such superstitions is somehow an impairment of freedom. Again, freedom is not freedom to cause or disseminate disease or freedom to deny scientific medical care to the ill.

When the politician understands the structure of medical practice, he will see the social inequity of the malpractice suit. Only the lawmaker who realizes that the present legal situation prevents doctors from trying new treatments for desperate diseases can be expected to

sponsor legislative relief. The politician must be inculcated with the facts about modern medical education, how comprehensive it must be, how expensive it is, so that he can plan practically to provide it. He must be impressed with the doctor's desire to keep his own house clean and his need for a medical practice act that will permit him to do so. The politician must have insight into the drug industry so as to be able to neutralize exploitation without hamstringing the development of new remedies.

An example of particular force at the present time is antivivisection legislation. There has been before the Senate Health Subcommittee a bill, S.3570, which would place such restrictions on the use of experimental animals in research laboratories as enormously to delay medical investigation. It is ironic that this measure was introduced by a liberal Senator and supported by other liberals. It was presented by John Sherman Cooper of Kentucky and co-sponsored by such men as William Proxmire of Wisconsin, Pat McNamara of Michigan, Estes Kefauver of Tennessee, Wayne Morse of Oregon, and Mike Mansfield of Montana. Only the statesman who is educated in the reality of animal experimentation can be expected to recognize the inadvisability of such legislation. Dr. Maurice B. Visscher writing in the *Humanist* pointed out years ago that we already have laws prohibiting cruelty to animals and that there is no need for obnoxious legislation that is based on the false premise that sadistic practices are now common, and that can be designed only to decrease the application of animal experimentation.

If doctors and other medical scientists were to attempt somehow to educate politicians, what would be the curriculum? And what would be the method of communication? It would seem, first of all, that every medical organization, be it a county society, a State association, the AMA, or a specialty group, should insist on regular and constant contact with the political powers of the city, county, state, and nation. Obviously, these societies must so conduct themselves as to earn the confidence of men of affairs. Their proposals must be such that they are clearly in the public interest and are not economically self-serving. Medical societies through their spokesmen, should be available to legislators at all times. Furthermore, they should not wait for invitations to give their opinions but should speak out openly whenever important questions arise that involve health. Professional associations should maintain liaison with the committees that direct legislation so that they can sponsor bills of their own, can back and second medically sound enactments proposed by others, and can fight on the proper committee battleground legislation which is definitely not in the interest of the public health. Organized medicine can go further. It can establish a relationship with the Governor of the State, the Mayor of a city, and other appointing officials so as to be considered a source of directive information when appointments involving doctors are made. Politicians by custom commission their friends and political creditors to office and are not easily persuaded to consider scientific accomplishment or medical competency when they look over the roster of physicians. We have seen exactly this situation in Arizona, where the appointive officers of the State have not asked ARMA for nominations of physicians for such bodies as the State Board of Public Welfare, a committee to study narcotic addiction, and a committee on atomic energy. The last two particularly distress us. The Association, at its 1960 Annual Meeting, sponsored a special seminar on the subject of narcotic addiction. Yet not one of the men who prepared that program was selected for the State Study committee. Not a single psychiatrist was appointed to evaluate a problem that is admittedly one involving emotional illness. And the committee was instructed, against all scientific thought on the subject, to "get tough" with drug law offenders. The Atomic Energy Committee was appointed without a radiologist member, nor was one picked until strong protests were lodged. ARMA promises a future attempt to convince the appointing officers that sound public policy dictates that this State Medical Association is the proper agency to consult whenever a physician is required for his special knowledge on a governmental commission or board.

Doctors should also enter into civic life at every possible point so that medical opinions will percolate upward from the grass roots toward the highest level of government. Physicians should be involved in civic committees, charitable agencies, school boards, and various voluntary organizations so that whenever a health question arises a doctor will be present to give enlightened guidance. We have only

ourselves to blame if we are not on the spot when we are needed. Our fellow citizens then either turn to uninformed persons or act impulsively on the basis of poor or ill-digested information. Every doctor, every year, all of his life, should be engaged in civic activity as partial fulfillment of his pledge to protect the public health.

There are also long-term ways in which medicine, like the other sciences, should attempt to influence government. A good case can be made out for a governmental Department of Medicine and a cabinet post for a doctor. The needs of health are not served by the present Department of Health, Education, and Welfare, nor would they be by a Department of Science. Medicine deserves a voice at the summit of government. Perhaps similar divisions should exist in our state governments, quite aside from the established departments of public health. Even more essential than this is public acquaintance with medical science. A. V. Hill, a great mind, once wrote, "Science is in the best sense, I believe, key to the whole culture of our modern world, that general culture which exists in its different and presently contesting forms along the Potomac, the Volga, and the Yangtze. But scientists are only the special professional exponents of their way. What will count in the end is not their acts alone nor their understanding of their duties, however deep, but the degree to which the general ends of science gain adherence among the people as a whole." If the informed public apprehends science it will in turn force the politician to foster legislation in the interests of science and in the interests of health. Such indoctrination is a medical society function. Perhaps there should be no public relations committee in a professional association, but only a public education committee. It is thus that your Association interprets the function of its public relations committee. It is oriented to informing the public about medical science, not to the advantage of the doctor's precious image but to the advantage of the health of the people. Finally, in the very longest view, doctors should demand adequate scientific medical education in the secondary schools and colleges, perhaps even in the elementary schools. A liberal education entails exact knowledge of man, and knowledge of man includes information about his physiological and emotional functionings and the fashion in which those processes become disordered. As a compulsory and non-elective part of education we should insist on hygiene, not to blow the doctors' trumpet, but to arm the people against the wiles of cultists, to teach them when and where to turn for help, to provide them with the background that will enable them to vote intelligently on social measures affecting medicine.

The public hungers for medical knowledge, and physicians must satisfy that hunger. We must satisfy it in the politician, in the adult public, and most essentially in our children. Some day organized medicine may publish its own periodical of opinion for the intelligent non-medical layman, a journal in its way like the *Bulletin of Atomic Scientists* and not merely a mass magazine like the AMA's present effort.

The task of the education of the politician is a grave charge on the doctor. The physician is pledged to preserve the public health; the politician legislates the facilities that implement the physician's promise. It is that simple. Alfred Korzybski put it this way: "The scientists, all of them, have their duties no doubt, but they do not fully use their education if they do not try to broaden their sense of responsibility toward all mankind instead of closing themselves up in a narrow specialization where they find their pleasure. Neither engineers nor other scientific men have any right to prefer their own personal peace to the happiness of mankind; their place and their duty are in the front line of struggling humanity, not in the unperturbed ranks of those who keep themselves aloof from life." This is a scientific and technical world. Modern knowledge in its best sense is largely scientific, and medicine is a part of science. Scientists by themselves, however, cannot achieve the indispensable ends.

Is this too big a job for the doctor? Its magnitude is really not the question. Rather is its necessity compelling. In the Twentieth Century, with modern knowledge of the causes of disease, physical and emotional, the education of the public, the education of the child, and expressly the education of the politician become inescapable and increasingly vital parts of the doctor's duty. The physician cannot in professional conscience evade this responsibility. It is a responsibility that your Association will not evade.

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Editorial

Radiation Control Legislation

It is a rare occurrence and worthy of comment when the Federal Government having once obtained control of some facet of our American living seems anxious to return that control to the states, where in most cases it rightfully belongs. Nevertheless at this time the Federal Government seems anxious to do this with regard to the control of ionizing radiation.

The Atomic Energy Commission which was born out of the necessity and emergency of a war time situation for the control of new and terrible forms of ionizing irradiation as exemplified by the atomic bomb also inherited by its very existence control over the peace time usages of newly discovered and developed forms of ionizing radiation. This has included the manufacture and distribution as well as usage of radio-active isotopes and other sources of radio-activity used in industrial, research, and medical fields.

Enabling legislation is now in existence and the AEC seems anxious to make use of this to

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CONTRIBUTIONS

The Editor sincerely solicits contributions of scientific articles for publication in ARIZONA MEDICINE. All such contributions are greatly appreciated. All will be given equal consideration.

Certain general rules should be followed, however, and the Editor therefore respectfully submits the following suggestions to authors and contributors:

1. Follow the general rules of good English or Spanish, especially with regard to construction, diction, spelling and punctuation.
2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.
3. Be brief, even while being thorough and complete. Avoid unnecessary words.
4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.
5. Manuscripts should be typewritten, double spaced, and the original and a carbon copy submitted.
6. Exclusive Publication — Articles are accepted for publication on condition that they are contributed solely to this Journal. Ordinarily contributors will be notified within 60 days if a manuscript is accepted for publication. Every effort will be made to return unused manuscripts.
7. Reprints will be supplied to the author at printing cost.

turn over to the states control of such peace time uses of these sources of ionizing irradiation and relinquishing their control as a federal organization.

In order to effect this transfer of responsibility a state must authorize its governor to sign an agreement with the Atomic Energy Commission assuming these responsibilities and control and the governor must satisfy the AEC that the state has set up a program including proper legislative authority, proper mechanism for inspection and licensing and proper means of enforcement which will be equivalent to or better than the existing AEC authority. If the governor satisfies the Atomic Energy Commission on these points the control will then be transferred to the state.

Most states have recognized that although the AEC is asking only controls over a small portion of the sources of ionizing irradiation that the whole situation presents a broader challenge and presents an opportunity for setting up adequate safety and health controls in regard to all sources of ionizing radiation which may be damaging to the health of the people or injurious to the general welfare. Some thought is then given to control of industrial and medical usages of x-ray equipment, the utilization of sources of ionizing irradiation which are not now under control of the AEC as for example, radium, the protection of workers in mining of radio-active ores, for example uranium, and possible rules and regulations in the transport of radio-active materials.

The problem which seems comparatively simple at first takes on additional complexities when a state anxious to exercise sufficient control for the protection of the health and other interest of its people finds that in adding controls for these purposes – it reaches a point where the beneficial use of such material is discouraged.

Honorable Paul Fannin, Governor of the State of Arizona, has appointed an Arizona Atomic Energy Committee whose purpose is to study this situation and to help draft proposed legislation to be presented to the next Legislature for action if possible. Two members of the Arizona Medical Association have been appointed to this Committee. They would be grateful, I am sure, for any suggestions or comments from the readers.

RLF

EDITOR'S NOTES
FOURTH NATIONAL CANCER CONFERENCE—1960

(IN TWO PARTS)
PART II

Lung Cancer – Lung cancer is the end stage of a series of sequential changes that require the presence of a carcinogenic agent, environmental host-modifying factors, and the inate susceptibility of the host.(42) A specific antigen to human lung cancer has been extracted.(44)

Those cancers arising from bronchial mucosa have a protracted latent and silent period. The change from bronchial metaplasia to carcinoma-in-situ to a silent shadow-casting lesion to a symptom-producing cancer is measured in years, not months.(41)

In only 10% of the patients with bronchiogenic cancer has the lesion been asymptomatic. In 90%, symptoms preceded radiological changes. Early detection must be designed to find the curable lung cancer, and the steps of early detection at present consist of semi-annual chest x-rays of the asymptomatic older male and adults with thoracic x-ray abnormalities.(13)

Cigarette smoking today is the single most important cause of bronchiogenic cancer in men. Other air pollutants play only a minor role.(39)

The cure rate of bronchiogenic carcinoma is 53% for local lesions. With lymph node involvement, this drops to 19%, and with evidence of invasion to 6%.(39)

Carcinoma of the Pancreas – There are only 14 recorded cases of 5-year survivals for carcinoma of the pancreas where the Whipple procedure was carried out. There is a 20% mortality for resection of the head of the pancreas for malignancy. The Whipple procedure and a palliative or short circuiting procedure have almost identical periods of survival following surgery, that is 9 months.(15)

Lymphomas and Leukemias – Hodgkin's Disease – as long as this is a local disease, treat it with deep x-ray therapy or surgery; surgery is probably preferable, possibly following it with

x-ray.(1) Supplemental chemotherapy as part of the initial control of advanced Stage II and Stage III lesions is usually desirable. Even in these, however, chemotherapy is not always necessary if the constitutional symptoms disappear during the course of irradiation therapy to all of the known sites. Reserve, if possible, chemotherapy for the terminal complications or for evidence of active disease in the absence of known localized activity. In lymphomas, in particularly Hodgkin's Disease, the patient's resistance is least disturbed, a longer remission is attained, and more complete rehabilitation of the patient procured with "local treatment for local disease."(36)

In 285 cases a survival rate has been attained of 25 years for 20% of the patients with a gradient up to 34% survival at 5 years. That is, four out of five become victims of recurrent disease. With local recurrences, irradiation should be as radical as treatment of the initial lesion was.(36)

Leukemia — Radiation exposure has been associated only with an increased incidence of myelogenous leukemia.(34)

There is an altered immune response and a hypogamma-globulinemia is a frequent concomitant of lymphoctytic leukemia.(34)

There is no good evidence that leukemia in man is viral in origin or that it is hereditary.(34)

Treat leukemia with the orally absorbed mustard compounds and the adrenal steroids. These two have greatly improved the effectiveness of therapy in chronic lymphatic leukemia. The patient feels better and life is extended. In chronic granulocytic leukemia, several groups of agents are effective in inducing temporary remissions; irradiation, myleron, the different mustard compounds, thiopurines and steroids are useful. When resistance to therapy does develop, all ordinarily effective agents have little or no benefit even though they are thought to have different mechanisms of action.(34)

There is a marked rise in leukemia in the age group over 60. There seems to be a sex predilection for the adult male. Therefore, one is forced to believe that there is a hormonal influence involved.(14)

Fifty percent of the patients who develop lymphosarcoma will develop leukemia.

In children who develop recurrent symptoms of intestinal obstruction, one should consider lymphosarcoma in the differential diagnosis.(14)

While 6-Mercaptopurine and Methotrexate are effective in leukemia, there is no indication that use of these drugs to the maximum tolerance dosage produces a higher remission rate than a lower level of usage.(42)

In nice, Methotrexate produced the greatest increase in survival time until compared with 3-Bromo-5-Chloroamethopterin and 3,5 Dichloroamethopterin which produce a survival time of 3-4 times as great.(42)

Cancer of the Stomach — A two weeks' medical trial is recommended for the ulcer. If this is found to be malignant, total gastrectomy is not recommended. Partial hepatectomy is recommended with invasion into one lobe. The results of using the colon as a substitute for the stomach are questionable.(23)

The uptake of radioactive phosphorus is 50% greater in cancer than in normal tissue. On the basis of this fact a test has been developed for gastric cancer whereby thin-walled ballons coated on the inside with an elastic latex base, which is photosensitive, are used. Twenty-four hours following the administration of 500 microcuries of P32, the balloon attached to a nasogastric tube is passed into the stomach, employing dark-room technique. The balloon is inflated with air, usually approximately 700 cc. The patient returns to the ward. Four to six hours later he is returned to the dark room for removal of the balloon. The radioautograph is developed using standard photographic techniques. With this procedure no false negative results were obtained. However, in 16 cases there were three false positives obtained. All of these were patients with healing gastric ulcers.(17)

Human tumor filtrates have shown an antigen specific to stomach cancer.(40)

Malignancy of the Small Intestine — 384 cases reviewed — 164 of them were sarcomas at an average age of 44.2 years; 175 carcinomas, average age 56.8 years; 45 carcinoids, average age 51.5 years. In an additional 39 cases recently reviewed, 25 were symptomatic. Three symptom complexes were noted: diarrhea with a mucus discharge, obstructive symptoms or gastrointestinal bleeding. The 5-year survival was 18% of patients with carcinoma, 20% in the presence of sarcoma, and only one case of carcinoid survived. The ileum was the most common site of

tumor formation of the small intestinal segments.(15)

Cancer of the Colon and Rectum – There has been some doubt cast on the etiologic relationship between polyps of the colon and cancer of the colon, for the distribution of the two is not the same. Empirically, polyps less than 2 cm. in diameter are not cancer.(16)

With cancer of the large bowl, 50% of the operated patients die in the first postoperative year, 13% the second postoperative year, 11% the third postoperative year, 8% the fourth postoperative year and 3% the fifth postoperative year. With each year follow-up, there is a greater approach to the expected normal survival, and after six years the patient does attain a normal survival rate.(17a).

Cancer of the Breast – There is a different rate of occurrence in the different countries; Japan 5/100,000, the United States 22/100,000, Denmark 24/100,000.

The mammotrops of the eosinophilic cells of the pituitary are important in the development of breast cancer.(2)

The artificial menopause has a protective effect to the development of breast cancer. There is a greater frequency in those who have never married or in those who married late in life. There is questionably a greater frequency in the woman who never nursed her babies. Cancer is probably associated with benign breast disease 3-5 times as frequently as it is present in the breast that has not had a benign lesion. The familial factor enters the incidence of breast cancer in that it is 2-3 times as frequent in those who are immediate blood relatives of those who have had breast cancer as it is in the general population.

The annual breast examination is of some help. In the routine examinations carried out, one cancer was found in every 553 examinations, or one cancer in every 150 patients examined. Two-thirds of these tumors were found on the second, third or a later follow-up visit. That is, they apparently developed or became of such size as to become detectable between examinations. Of the asymptomatic patients with cancer, three of the 21 had positive nodes. Of the symptomatic patients, 82% had a 5-year survival. The asymptomatic patients had 100% survival for 5 years.(5)

A number of tumors were found in patients who had been doing breast self-examinations. Therefore, one must very seriously question the value of this procedure.(5)

In the treatment of breast cancer, should we judge our success of treatment by 5-year survival or by the prolongation of comfortable life?(7)

There is a long duration of the tumor being in existence prior to its recognition. If one studies the time for a tumor to double in size in a study of chest metastases, the tumor that doubles in size in 55 days had its inception approximately 5 years ago. The tumor that doubles in size in 76 days had its start eight years ago. The tumor that doubles in size in 121 days arose from malignant cells 10 years ago.(7)

Hormones in the treatment of advanced carcinoma of the breast – if one fails in the use of one class of hormones, you should shift the class, i.e., from estrogens to androgens, or vice versa, in association or not with adrenal-corticoids.(8)

With soft tissue and lung metastasis in the female more than five years post-menopausal, use large doses of estrogen. The androgens are less site specific. The liver and central nervous system give poor response. Remissions are shorter with androgens than with the use of estrogens.(8)

If testosterone is used, use initially 100 mgm. three times per week. It is usually noted with the greater the time the patient is post-menopausal, the greater the response noted to testosterone. 2-Methyl-Dihydro-Testosterone Proprionate is probably as effective in tumor suppressive action with less masculinizing effect. (18)

Estrogens can be given safely in the immediate post-menopausal female.(18)

Ablative procedures – initially oophorectomy is indicated for disseminated disease. If the patient had a satisfactory response to oophorectomy, then adrenalectomy is more likely to be helpful, after you lose control of the patient or lose the suppressive effect from the oophorectomy. If the patient is more than two years menopausal, if estrogen gives some response after you lose control with the estrogen, also use adrenalectomy. If the patient did not respond to androgens, there is no criteria if adrenalectomy will be helpful. However, the longer the free period before there is evidence of recu-

rence, the more likely there is to be an objective regression with an ablative procedure,(9) as oophorectomy, adrenalectomy or hypophysectomy.

The question of castration brings up a number of debatable points. If the patient is still menstruating, castration produces the greatest percentage of remissions for the longest periods of time. However, cancer of the breast proceeds in spurts. It should be treated only during a period of advance in the disease. If there is an advance in the disease after castration, or in the post-menopausal period, use Testosterone Propionate. After obtaining a remission with Testosterone Propionate, or failing to do so, wait after stopping the drug before starting another. The patient may have a remission as a result of the withdrawal. When the disease advances again, give estrogen therapy. Then when control is again lost, treat with corticosteroids. After above treatment, and only then, are ablative procedures indicated as adrenalectomy and hypophysectomy.(18)

There have been approximately 9% postoperative deaths following either adrenalectomy or hypophysectomy. There has been objective regression in 32% of the cases after adrenalectomy and 30% after hypophysectomy. The period from ablative procedure to death has averaged 7.6 months following adrenalectomy and 6.5 months following hypophysectomy. These two procedures have given almost equal results with metastasis to bone, soft tissue or viscera. The question arises – does the replacement corticosteroid do some or all of the effective work that is noted from this ablative procedure?(9) It possibly and probably does.

The question arose of prophylactic versus therapeutic castration. Twenty-five percent of patients will show improvement in the premenopausal female with recurrence and given an oophorectomy. Therefore, it is probably indicated to carry out a prophylactic castration in the premenopausal female and in the female up to two years after menopause. It may result in a greater survival rate and a greater duration of survival. The use of irradiation as a castration method is probably less effective than surgical oophorectomy. Prophylactic castration is probably to be encouraged. One should be guided by the degree of disease present. In the patient with extensive disease, prophylactic castration may be of significant help.(24)

Chemotherapeutic agents in breast cancer – there is a difference of opinion as to the most effective drug available. Thio-tepa is preferred by some.(8) 5-Fluorouracil by others.(16a)

The chemotherapeutic agent should be reserved for thos who don't respond to hormones. The Fluoropyrimidines have resulted in some regressions, but they are extremely toxic. The question has arisen but is not proven – is there a greater survival if Thio-tepa is given in the immediate postoperative period?(8)

Mitomycin C has some effect in breast cancer. A lower total dosage with greater effect is noted if given every four days.(16a)

Supraradical mastectomy – parasternal recurrence occurs in approximately 10% of the medial and central lesions treated by radical mastectomy. If the supraradical procedure is done properly, this is the group that is eliminated. This procedure should probably be applied to the clinically operable lesions presenting in the central and medial portions of the breast. It is a difficult procedure and should be done only under ideal circumstances. However, 15% of the patients with no evidence of metastasis to the axilla had positive internal mammary nodes. If the axilla was positive, 55% had positive internal mammary nodes. The overall picture is for 33% to show internal mammary node involvement. Therefore, the internal mammary chain should be treated as aggressively as the axilla. If that is done, the cure rate is probably increased 8-10%. Mortality rates are not greater than those with the usual radical mastectomy.

The 5-year survival is 63% with the standard radical mastectomy, a 57% 5-year salvage that is clinically free, 10-15% have a local recurrence. McWhorter apparently has approximately a 19% local recurrence rate. Thirty-eight percent of all patients with internal mammary involvement are free of disease at 5 years. And when only the internal mammary nodes are involved, 44% are free at 5 years. The local recurrence rate is 8%.(6)

Others have not been so satisfied with the supraradical mastectomy, feeling that it is actually detrimental as has been supra-voltage x-ray.(11)

If a supraradical mastectomy is done, fascia lata or ox fascia may be used as a graft to correct the defect.

The survival ratio for patients who have had cancer of the breast, and it was a localized breast

carcinoma, remains below average, approximately 2-4% below the average survival rate even 15 years after the diagnosis and treatment carried out. Thirty-four percent are alive 15 years after surgery. The normal survival rates would indicate that 61% should be alive.(17a)

Cancer of the Thyroid – Seventy percent of the patients dying of cancer of the thyroid and under 17 years of age have had irradiation in the area of the neck. In 80% of the cases this was to the thymus. The thyroid gland in the child is markedly more sensitive to irradiation than in the adult. Even light doses of irradiation to the neck region may result in a thyroid malignancy.(20).

The average dose given these children was 500 r, and the average length of time was eight years from the stimulating dose to the time of development of the malignancy. There is no evidence that I_{131} has caused any case of cancer of the thyroid.(22)

The first barrier to spread of cancer of the thyroid is the capsule; secondly, the nodes on the capsule; and third, finally, the jugular nodes and suprasternal nodes.(22)

Twenty-two percent of the cancers are papillary carcinoma, 5% follicular, 6% solid, and 67% are mixed of two of the above types. Fifty-three percent had adenomas, but none of the cancers arose in an adenoma. Eighty-eight percent of the patients showed bilateral dissemination. In only two of 60 cases studied was there blood vessel invasion.(22)

From the above it would seem that a bilateral total thyroidectomy is indicated but not a prophylactic neck dissection. The dissemination of thyroid cancer outside of the lymph nodes by continuity is rarely seen unless it contains components of solid tumor or is sarcomatous in type.(22)

Radioactive iodine as a scanning procedure is inadequate as a diagnostic means for thyroid nodules. Only 20% of the cancers pick up iodine. They are the follicular and alveolar types. P_{32} is not diagnostic. There is no substitute for removing the nodule. The possibilities of cancer being present in a nodule that does not show activity (cold nodule) are greater than if the nodule shows activity (hot nodule).(33)

If a patient is to receive irradiation for malignancy of the thyroid, say an inoperable patient, as much of this thyroid tissue should be removed as possible before starting irradiation therapy.(21)

Cancer of the Male Genital Tract – The incidence of cancer of the bladder is two times as great in cigarette smokers. Treat the prostatic cancer with radical perineal prostatectomy and/or hormonal therapy. Five percent are potentially curable when first seen. Over 50 years of age, the male should have a yearly rectal examination of the prostate.

In patients who have had maximum antiandrogenic therapy with a good response and a later relapse, further treatment with steroids is advocated. Similar results are obtained by "medical adrenalectomy" by the administration of cortisone as by adrenal ablation.(30)

Sarcolysin has a very definite effect on the group of tumors called the seminoma and with the associated metastasis. It has no effect on other testicular tumors as chorioepithelioma, teratoma and sarcoma. Primary tumors are usually less sensitive to chemotherapy as compared with metastasis. Therefore, surgical treatment should be combined with chemotherapy. There should be pre- and postoperative administration of Sarcolysin. Treatment with this agent leads to the complete disappearance of all tumor metatasis in 50% of the cases of seminoma.(40)

This treatment consists of 40-50 mgm. once in 6-7 days. The blood must be watched constantly for leukopenia. If treatment is successful, repeated treatment must be carried out at intervals in reduced dosage to prevent relapse.(40)

Others advocate the use of radiotherapy for seminomas since they are radio-sensitive in 40% of the cases.(27)

Carcinoma of the Female Genital Tract – Human smegma is unquestionably carcinogenic. It certainly is in laboratory animals.

Routinely do Pap stains every year on all females over 40 years of age.

The expected 5-year survival rate for carcinoma of the vulva is 70%, for carcinoma of the vagina 25%, carcinoma of the cervix 55%, carcinoma of the endometrium 70% and carcinoma of the ovary 25%.

Choriocarcinoma is treated successfully in approximately one-third of the cases with Methotrexate. In these cases complete regression is obtained.(42)

Carcinoma of the endometrium in a number

of cases has responded with progestational agents.(18)

Resection of the Liver – has been done in a few cases for metastasis, but few tumors are amenable to this procedure. Possibly some cases of cancer of the colon have a resectable liver metastasis. If there is direct invasion, a resection of that segment of the liver can be carried out. The mortality is 30-40% for this procedure.

Chemotherapy – There are now 109 drugs in various stages of clinical evaluation. These include 53 steroids and hormones, 22 alkylating agents, 8 antibiotics, 16 antimetabolites and 10 miscellaneous agents.(42)

A method of total body perfusion has been developed and utilized in treating disseminated cancer. Isolation perfusion techniques have been more successful, and five drugs have been used. These included nitrogen mustard, phenylalinine mustard, actinomycin D, TSPA and 5-Fluorouracil. Complications are edema of the extremity, depression of hemopoesis and gastrointestinal upset.

5-Fluorouracil has shown effective response in solid tumors if used until stomatitis and diarrhea appear. Objective remissions have been noted in cancer of the colon, breast, rectum, cervix, ovary and liver, with no effect in cancer of the lung, stomach, pancreas and malignant melanoma.(42)

Sarcolysin has shown effective results in seminoma, reticulum cell sarcoma and Ewing's tumor.(16a)

The chemotherapeutic index of nitrogen mustard is 1.1:1; for Cytoxan it is 3.4:1. Some of the acute leukemias have been responsive to Cytoxan when they are no longer responsive to nitrogen mustard. Bronchiogenic carcinoma can probably be aided by the use of Cytoxan.(16)

Survival – (5-Year Survival)(17)

	1935-1944	1945-1954
Breast	76%	78%
Corpus uterus	68%	81%
Cancer of the cervix	52%	67%
Cancer of the ovary	52%	66%
Cancer of the large bowel	37%	64%
Cancer of the rectum	30%	52%
Cancer of the stomach	13%	21%

Patients treated for cancer of the lung before demonstrable spread beyond the lung show a salvage rate greater than 50%.(17)

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42. National Cancer Institute, Bethesda, Md.
43. Wendell M. Stanley, Virology, University of California, Berkeley, Calif
44. James T. Grace, Jr., Roswell Park Memorial Institute, Buffalo, N. Y.

LETTER TO THE EDITOR

September 24, 1960

My dear Friend,

I was very glad to receive your letter in which you show me your anxiety about the future of the medical practice in the States.

But, in spite of this shadowy horizon, I have made up my mind to come back to North America, this time in the States.

The American Consul in Marseille told me this afternoon the way to obtain quickly an immigrant visa; I must give him a letter of an American approved hospital, by which my services as an intern are needed urgently.

And, walking back to my office, I thought that it would be very pleasant for me (and I hope, not too disagreeable for you) to work as an intern in your hospital. It would be a good opportunity for us to meet and know better each other.

Don't consider me as a joker; I know perfectly what I want and if we are back to France, it is not completely my fault. When poor Yolande reminds our Canadian experience, she begins shivering and her nose grows red retrospectively. You know as much as we do about cold regions, don't you?

And, to be frank, we strongly prefer the U. S. manners than the Canadian ones, even in Quebec.

I have not the formal intention to practice in Tucson after the five years required for the American citizenship, but probably in a little sunny town. You are quite unable to conceive the French medical situation; for example, I tell you how much we are obliged to charge in application of the new laws: last week, I had three private operations: a peritonitis by perforated appendix, 36 dollars: an hysterectomy, 72 dollars a perineorraphy with ablation of a big left ovary cyst, 86 dollars, that is to say 194 dollars including forty visits after those operations. We are indeed obliged to attend freely an operated patient during a period of 21 days.

But the main reason of my desire to move to the States is that I consider as very problematic my children's future situation in France; we are now as a boiling pot with the people coming back to France from our "ex-colonies" and it is to become mad when we see the rush of the children in the schools of all kind.

That are the reasons why I will not stay longer in France, even on the "Cote d'Azur"; I suppose easily that your future conditions of working will be better than those above mentioned.

I much appreciate your non interference in the other man's business but I strongly ask you as a personal service to help me in this way. Can you tell me how much an intern is paid usually in the States and especially in Tucson hospital. In spite of our Canadian experience, we have still a pretty lot of money that will help us to live almost comfortably during five years.

I hope your answer very soon and, expecting your letter, I send you my best wishes for you and your family.

Sincerely yours,
Dr. Y. H. Wuidart

N-B. — You don't know very much about myself and my studies.

I am now forty-one and have been graduated from Paris Medical University (1946).

I have learned surgery in the Paris Hospitals where I was the assistant of professor Antonin Gosset.

Chief surgeon of Red-Cross Maternity.

Since 1946, I practiced private surgery and I am very interested in gynecology and cancer.

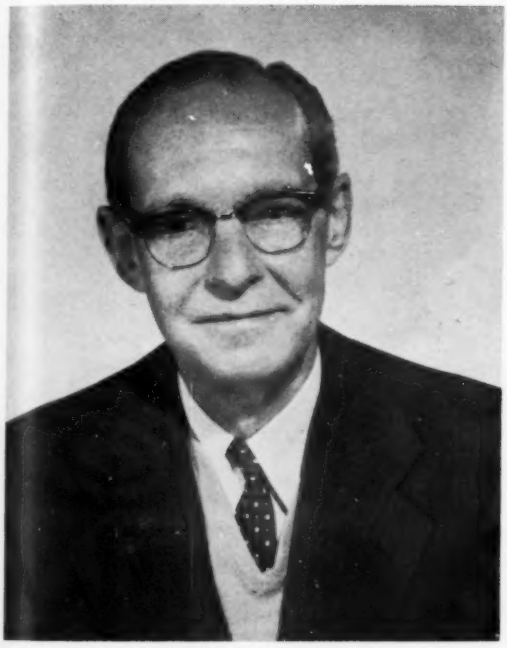
I published some personal works about cancer in French publications and one in a Canadian journal of surgery about porphyries.

If necessary, I should send to the hospital the photostatic copies of my diplomas and certificates.

In Memoriam

Howard Currie James

1906 - 1960



Howard C. James, M.D.

Dr. Howard Currie James died at St. Mary's Hospital, October 18, 1960. He was born in Laurium, Michigan, May 23, 1906. He practiced obstetrics and gynecology in Tucson for over twenty-five years.

Dr. James was married in 1930 to Dorothy Rice of Delaware, Ohio. A daughter, Mrs. C. Dee Simpson of Phoenix and a son, Michael, a student at DePauw University were born of this marriage. Two grandchildren also survive.

Dr. James received his bachelor's degree from Ohio Wesleyan University and his doctor of medicine degree from Michigan University. Dr. James served as intern at Manhattan Maternity Hospital in 1932 and he served a rotating internship at Moses Taylor Hospital, Scranton, Pennsylvania, in 1933. He was a resident at Chicago Lying-In Hospital in 1934. He practiced his specialty in Tucson from 1935 until his death.

Dr. James was a member of Phi Gamma Delta social fraternity and Nu Sigma Nu medical fraternity and a member of the Pima County Medical Society. He was president of the Tucson Obstetrical and Gynecological Society in 1956. He was Vice President of St. Mary's Hospital Staff in 1944. He was president of the staff in 1950 and 1951. He was a member of the governing staff in 1955. He was a member of the Arizona Medical Association and the American Medical Association. He was a fellow of the American College of Surgeons, the Southwestern Obstetrical and Gynecological Society and the Central Obstetrical and Gynecological Society. He was a member of the American Academy of Obstetrics and Gynecology.

Dr. James was called "Mike" nearly all of his life. This name he received from his father when he was a little boy. The name stuck and I think that even Dr. James forgot that "Mike" was not his given name.

Dr. James delivered over six thousand babies and there were no maternal deaths. These remarkable statistics represent a doctor's life and devotion to his work. This high standard of personal and professional response to the practice of medicine is a final salute to a great doctor.

B. P. Storts, M.D.

Available only to physicians for their distribution—

Complete Cholesterol Depressant Menus and Recipe Book

A new, authoritative patient-aid . . . for professional distribution only

Now available for use in your practice from The Wesson People . . . easy-to-use manual of 40 pages, including all necessary diet instructions . . . menus, recipes, shopping and cooking guidance . . . all worked out for you . . . so arranged and printed that you have only to check the desired daily calorie level before giving the book to your patient.

You will find this book invaluable for treating patients with elevated serum cholesterol.

Complete menus for 10 days enable you to prescribe diets which are appetizing, nutritiously adequate and which can exert cholesterol depressant activity. Special attention has been given to constructing the menu patterns so that they adhere as closely as permissible to the patient's normal eating habits.

NRC Standards fulfilled. Each menu has been calculated to provide the proper daily allowance of proteins, vitamins and other nutrients as recommended by the Food and Nutrition Board of the National Research Council.

Weight control is achieved as each day's menu is given at 3 calorie levels—1200, 1800 and 2600 calories. You prescribe the level most desirable and modify as desired.

Variety and appetite appeal for patient are built into the menu plan to an extent not previously accomplished. Alternate choices for main dishes minimize monotony, encourage the patient to follow closely the menu plan you specify.

Complete recipes—65 in all—are included to assure that the specified menus provide prescribed levels of calories, the pre-determined ratio of poly-unsaturated to saturated fat, plus essential nutrients.

Dietary fat is controlled so that approximately 36% of the total calories are derived from fat and at least 40% of these fat calories are from poly-unsaturated components (linoleates) as found in pure vegetable oil. The replacement of saturated dietary fat by this percentage of poly-unsaturated fat has been found in clinical studies most effective in the reduction of serum cholesterol and in its maintenance at desirable levels. More liberal menus are provided for maintenance after the patient's progress indicates that desired therapeutic results have been accomplished.

Family meal preparation is simplified. The menus are planned around favorite foods having wide appetite appeal for all members of the household. Patients can entertain in comfort—enjoy cakes, cookies, snacks, prepared with recipes which meet medical requirements.

A high degree of satiety is achieved even at the lower calorie levels, because Wesson provides an unexcelled source of concentrated, slow-burning food energy.

Adaptable for use with diabetics. Carbohydrates have been calculated to fall within the acceptable range for patients to whom a diet planned for diabetes is important. Calories, which must be supplied from fat when the carbohydrate intake is limited, are provided by desirable poly-unsaturated vegetable oil.

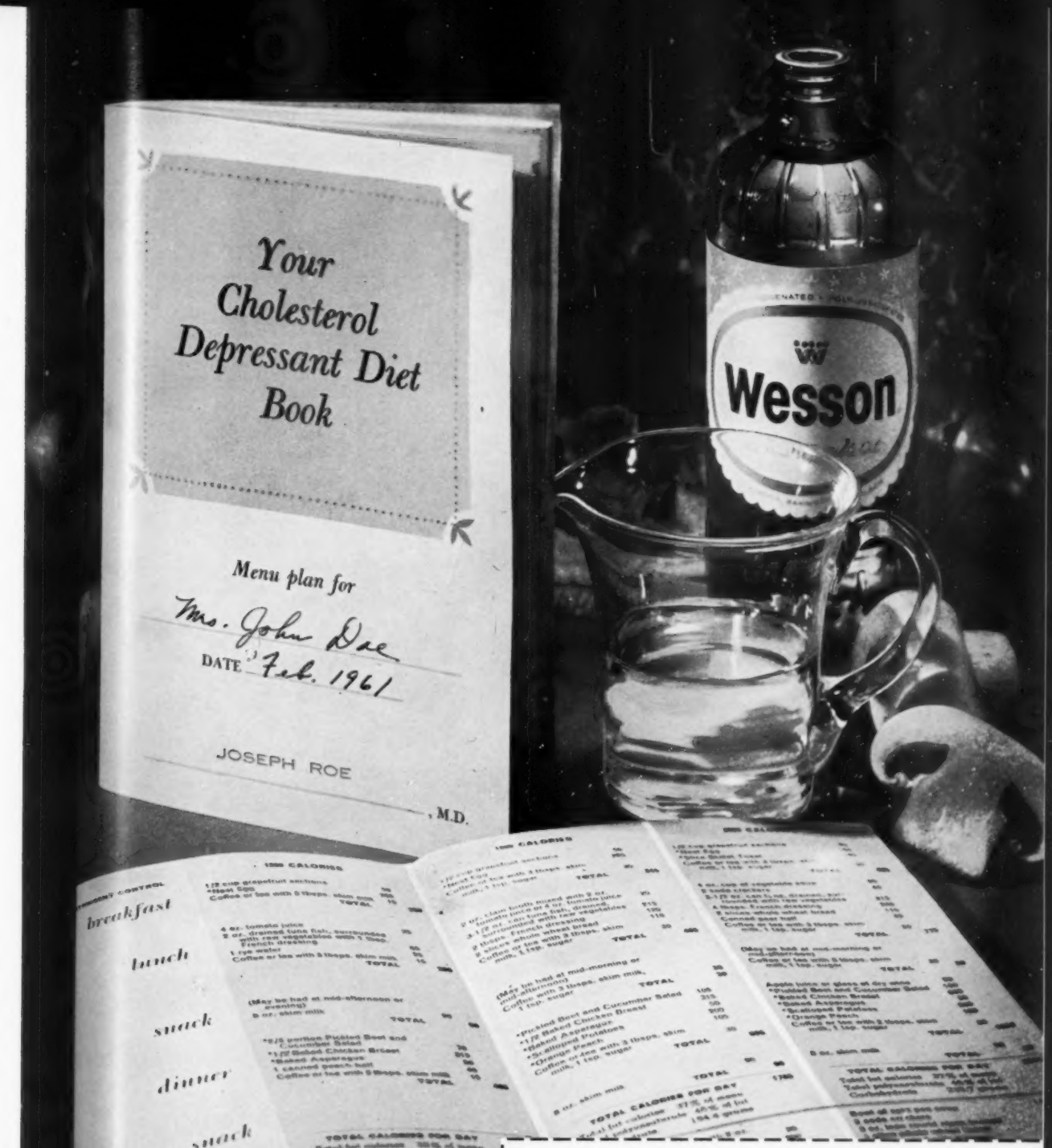
WESSON'S IMPORTANT CONSTITUENTS

Wesson is 100% cottonseed oil—winterized and of selected quality

Linoleic acid glycerides (poly-unsaturated)	50-55%
Oleic acid glycerides (mono-unsaturated)	16-20%
Total unsaturated	70-75%
Palmitic, stearic and myristic glycerides (saturated)	25-30%
Phytosterol (Predominantly beta sitosterol)	0.3-0.5%
Total tocopherols	0.09-0.12%

Never hydrogenated—completely salt free

Poly-unsaturated Wesson is unsurpassed by any readily available brand, where a vegetable (salad) oil is medically recommended for a cholesterol depressant regimen.



Topics of Current Medical Interest

Board of Medical Examiners State of Arizona

The Board of Medical Examiners of the State of Arizona at a regular meeting held Saturday, October 15, 1960, issued certificates to practice medicine and surgery in this State to the following doctors of medicine:

ALLEN, Glen Ivan (I), 600 1st Nat'l Bank Bldg., Peoria, Ill.

BAUER, Thomas William (Oph), 550 West Thomas Road, Phoenix, Arizona.

BAUMGARTNER, JR., Donavin Albert (GS), 15660 Oakhill Rd., East Cleveland, Ohio.

BOCK, George Edward (I), Sedona, Arizona.

BRUST, Richard Duane (GP), 130 Monroe St., Nogales, Arizona.

BURCH, John Ellis (ObG), 200 Medical Arts Bldg., Joplin, Missouri.

CARROLL, Daniel Bear (PlReS), 644 Post Avenue, Rochester, New York.

CLEMANS, III, William Joseph (GP), 1518 Main St., Florence, Arizona.

COHEN, Sidney A. (Path), Edmundson Hospital, Council Bluffs, Iowa.

DUDLEY, Patrick William (GP-I), 6042 W. Pinchot Avenue, Phoenix, Arizona.

FLOYD, Alfred Robert (Oph), Lackland AFB Hosp., Lackland AFB, Texas.

FRENCH, Alfred Robert (Oph), 722 Professional Building, Phoenix, Ariz.

FUZZELL, Jameso (ObG), Maricopa Co. Gen. Hosp., Phoenix, Ariz.

HAGGARD, Jerry Wayne (GP), 4752 E. Indian School Rd., Phoenix, Ariz.

HARDIN, Oscar Allen (ObG), 1200 E. Washington Street, Phoenix, Ariz.

HARE, Renate Zeissler (GP), 7603 N. 19th Avenue, Phoenix, Arizona.

HAYWARD-BUTT, John Terry P. (Anes), 5713 N. 11th St., Phoenix, Arizona.

HENDRICKSON, Charles William (A), 2515 North Main St., Santa Ana, Calif.

HINDMAN, William McIntosh (Path), 1641 N. Tucson Blvd., Tucson, Arizona.

HUTH, Peter Emery (U-GP), 3408 East Fairmount Ave., Tucson, Ariz.

KENNEDY, Joseph Mathias (GP-I), Maricopa County Gen. Hosp., Phoenix, Ariz.

KNOX, Jasper Newman (GP), PHS Indian Hosp., Parker, Arizona.

LINDBERG, Robert Dery (R), 721 North 4th Avenue, Tucson, Arizona.

LIST, JR., Ellis Worthington (GP), McNary Hospital, McNary, Arizona.

MOON, Barclay Jay (GP-Ind), 1756 1st Ave., N.E., Cedar Rapids, Iowa.

MOORE, Thomas Francis (GP), Miami-Inspiration Clinic, Miami, Arizona.

OSTEGAARD, Erling (GP), Rock Point Mission Hospital, Chinle, Ariz.

RUDOLPH, JR., Royal William (Anes), Craycroft Med. Center, Tucson, Arizona.

SCHERER, Roland Gustav (U), 114 East Main St., Bozeman, Montana.

SCHREIBER, Norman John (GP), 618 South 5th St., St. Charles, Illinois.

SMITH, Clinton Russell (I), 4250 E. Thomas Road, Phoenix, Arizona.

SMITH, Richard Lee (GP), 550 N. Country Club Dr., Mesa, Arizona.

TAYLOR, Lawrence Carol (S), 1905 E. Fairview Ave., Park Ridge, Ill.

THOMAS, H. Stephens (GP), Harbor General Hosp., Torrance, Calif.

WEBER, Johan Otto (Pd), St. Joseph's Hosp., Phoenix, Arizona.

WEISTENTHAL, Charles Leonard (U), 945 N. 12th, Milwaukee, Wisconsin.

WERTZ, Max Lindbergh (Otol), 222 E. Delaware, Chicago 11, Illinois.

YARD, George Harges (GP), 914 Meade, Flagstaff, Arizona.

ZAGER, Lewis Llewellyn (S), 927 W. Fourth St., Waterloo, Iowa.

if you're treating a coccal infection... you can't prescribe a more effective antibiotic than ERYTHROCIN

Erythromycin, Abbott

How much "spectrum" do you need in treating an infection? Clearly, you want an antibiotic that will show the greatest activity against the offending organism, *and the least activity against non-pathogenic gastro-intestinal flora.*

Weigh these criteria—and make this comparison—when treating your next coccal infection. Erythrocin is a medium-spectrum antibiotic, notably effective against gram-positive organisms. In this it comes close to being a "specific" for coccal infections—*which means it is delivering a high degree of activity against the majority of common infection-producing bacteria.*

And against many of the troublesome "staph" strains—a group which shows increasing resistance to penicillin and certain other antibiotics—Erythrocin continues to provide bactericidal activity. Yet, as potent as Erythrocin is, *it rarely has a disturbing effect on normal gastro-intestinal flora.* Comes in easy-to-swallow Filmtabs®, 100 and 250 mg. Usual adult dose is 250 mg. every six hours. Children, in proportion to age and weight. Won't you try Erythrocin?

®Filmtab—Film-sealed tablets, Abbott.

ABBOTT

ANNOUNCING—
SPECIFICALLY FOR
INFECTIONS DUE TO
"RESISTANT" STAPHYLOCOCCI

AN ENTIRELY NEW SYNTHETIC
"STAPH-CIDAL" PENICILLIN

Staphcillin™

sodium dimethoxyphenyl penicillin
FOR INJECTION

UNIQUE—BECAUSE IT
RETAINS ANTIBACTERIAL
ACTIVITY IN THE PRESENCE OF
STAPHYLOCOCCAL PENICILLINASES
WHICH INACTIVATE
OTHER PENICILLINS

Bristol™

NEW SYNTHETIC PENICILLIN FOR "RESISTANT" STAPH

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UNIQUE SYNTHETIC "STAPH-CIDAL" PENICILLIN

OFFICIAL PACKAGE CIRCULAR
November, 1960

STAPHCILLIN™

(sodium dimethoxyphenyl penicillin)

For Injection

DESCRIPTION

STAPHCILLIN is a unique new synthetic parenteral penicillin produced by Bristol Laboratories for the specific treatment of staphylococcal infections due to resistant organisms. Its uniqueness resides in its property of resisting inactivation by staphylococcal penicillinase. It is active against strains of staphylococci which are resistant to other penicillins.

Each dry filled vial contains: 1 Gm. STAPHCILLIN (sodium dimethoxyphenyl penicillin), equivalent to 900 mg. dimethoxyphenyl penicillin activity.

INDICATIONS

STAPHCILLIN is recommended as specific therapy only in infections due to strains of staphylococci resistant to other penicillins, e.g.:

Skin and soft tissue infections: cellulitis, wound infections, carbuncles, pyoderma, furunculosis, lymphangitis and lymphadenitis.

Respiratory infections: staphylococcal lobar or bronchopneumonia, and lung abscesses combined with indicated surgical treatment.

Other infections: staphylococcal septicemia, bacteremia, acute or subacute endocarditis, acute osteomyelitis and enterocolitis.

Infections due to penicillin-sensitive staphylococci, streptococci, pneumococci and gonococci should be treated with Syncillin® or parenteral penicillin G rather than STAPHCILLIN. Treponemal infections should be treated with parenteral penicillin G.

DOSAGE AND ADMINISTRATION

STAPHCILLIN is well tolerated when given by deep intragluteal or intravenous injection.

As is the case with other antibiotics, the duration of therapy should be determined by the clinical and bacteriological response of the patient. Therapy should be continued for at least 48 hours after the patient has become afebrile, asymptomatic and cultures are negative. The usual duration has been 5-7 days.

Intramuscular route: The usual adult dose is 1 Gm. every 4 or 6 hours. Infants' and children's dosage is 25 mg. per Kg. (approximately 12 mg. per pound) every 6 hours.

Intravenous route: 1 Gm. every 6 hours using 50 ml. of sterile saline solution at the rate of 10 ml. per minute.

**Warning:* Solutions of STAPHCILLIN and kanamycin should not be mixed, as they rapidly inactivate each other. Data on the results of mixing STAPHCILLIN with other antibiotics are being accumulated.

DIRECTIONS FOR RECONSTITUTION

Add 1.5 ml. sterile distilled water or normal saline to a 1 Gm. vial and shake vigorously. Withdraw the clear, reconstituted solution (2.0 ml.) into a syringe and inject. The reconstituted solution contains 500 mg. of STAPHCILLIN per ml. Reconstituted solutions are stable for 24 hours under refrigeration.

For intravenous use, dilute the reconstituted dose in 50 ml. of sterile saline and inject at the rate of 10 ml. per minute.

*This statement supersedes that in the Official Package Circulars dated September and/or October, 1960.

(continued)

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MICROBIOLOGICAL AND PHARMACOLOGICAL PROPERTIES

In vitro studies show that STAPHCILLIN is a bactericidal penicillin with activity against staphylococci resistant to penicillin G. Strains of staphylococci so far tested have been sensitive to STAPHCILLIN *in vitro* at concentrations of 1-6 mcg. per ml. These levels are readily attained in the blood and tissues by administration of STAPHCILLIN at the recommended dosage. This unique attribute is probably due to the fact that STAPHCILLIN is stable in the presence of staphylococcal penicillinase. STAPHCILLIN also resists degradation by *B. cereus* penicillinase. The antimicrobial spectrum of STAPHCILLIN with regard to other microorganisms is qualitatively similar to that of penicillin G; but considerably higher concentrations of STAPHCILLIN are required for bactericidal activity than is the case with penicillin G.

STAPHCILLIN is rapidly absorbed after intramuscular injection. Peak blood levels (6-10 mcg./ml. on the average after a 1.0 Gm. dose) are attained within 1 hour; and then progressively decline to less than 1 mcg. over a 4 to 6 hour period. It is poorly absorbed from the gastrointestinal tract. STAPHCILLIN is rapidly excreted by the kidney.

As shown by animal studies, STAPHCILLIN is readily distributed in body tissues after intramuscular injection. Of the tissues studied, highest concentrations are reached in the kidney, liver, heart and lung in that order; the spleen and muscles show lower concentrations of the antibiotic. STAPHCILLIN diffuses into human pleural and prostatic fluids, but its diffusion into the spinal fluid has not yet been completely studied. However, one patient with meningitis showed a significant concentration in his spinal fluid while on STAPHCILLIN therapy.

Toxicity studies with STAPHCILLIN and penicillin G in animals show that they have approximately the same low order of toxicity.

Certain staphylococci can be made resistant to STAPHCILLIN in the laboratory, but this resistance is not related to their penicillinase production. During the clinical trials, no STAPHCILLIN-resistant strains of staphylococci were observed or developed; the possibility of the emergence of such strains in the clinical setting awaits further observation.

PRECAUTIONS

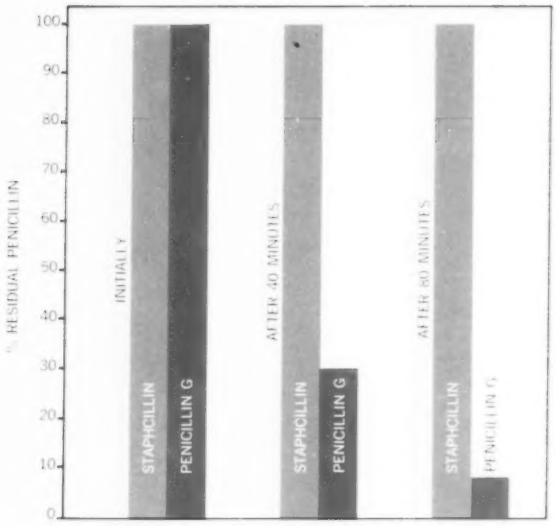
During the clinical trials, several mild skin reactions, e.g., itching, papular eruption and erythema were observed both during and after discontinuance of STAPHCILLIN therapy. Patients with histories of hay fever, asthma, urticaria and previous sensitivity to penicillin are more likely to react adversely to the penicillins. It is important that the possibility of penicillin anaphylaxis be kept in mind. Epinephrine and the usual adjuvants (antihistamines, corticosteroids) should be available for emergency treatment. Because of the resistance of STAPHCILLIN to destruction by penicillinase, parenteral *B. cereus* penicillinase may not be effective for the treatment of allergic reactions. Information with regard to cross-allergenicity between penicillin G, penicillin V, phenethicillin (Syncillin) and STAPHCILLIN is not available at present. If superinfection due to Gram-negative organisms or fungi occurs during STAPHCILLIN therapy, appropriate measures should be taken.

SUPPLY

List 79502 — 1.0 Gm. dry filled vial.

BRISTOL LABORATORIES • SYRACUSE, NEW YORK
Division of Bristol-Myers Company

UNIQUE SYNTHETIC "STAPH-CIDAL" PENICILLIN



In the presence of staphylococcal penicillinase, STAPHCILLIN remained active and retained its antibacterial action. By contrast, penicillin G was rapidly destroyed in the same period of time. *(After Gourevitch et al., to be published)*

Specifically for "resistant" staph...

Staphcillin

sodium dimethoxyphenyl penicillin
FOR INJECTION

The failure of staphylococcal infections to respond to penicillin therapy is attributed to the penicillin-destroying enzyme, penicillinase, produced by the invading staphylococcus.

Unlike other penicillins:

1 STAPHCILLIN is effective because it retains its antibacterial activity despite the presence of staphylococcal penicillinase.

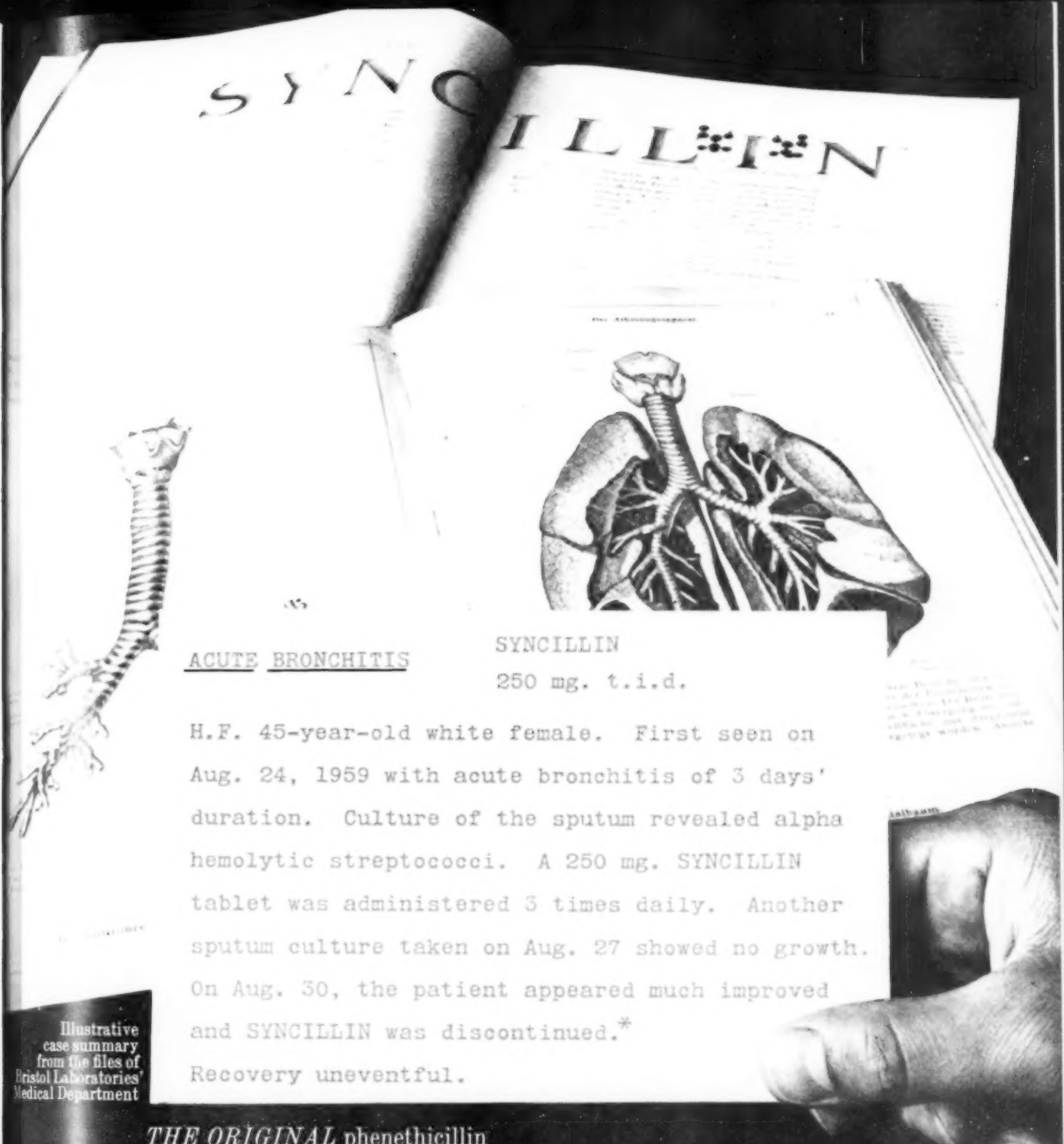
2 The clinical effectiveness of STAPHCILLIN has been confirmed by dramatic results in a wide variety of infections due to "resistant" staphylococci, many of which were serious and life-threatening.

Like other penicillins:

STAPHCILLIN has no significant systemic toxicity. It is well tolerated locally, and pain or irritation at the injection site is comparable to that following the injection of penicillin G. *In occasional cases, typical penicillin reactions may be experienced.*

PROFESSIONAL INFORMATION SERVICE — The attached Official Package Circular provides complete information on the indications, dosage, and precautions for the use of STAPHCILLIN. If you desire additional information concerning clinical experiences with STAPHCILLIN, the Medical Department of Bristol Laboratories is at your service. You may direct your inquiries via collect telephone call to New York, PLaza 7-7061, or by mail to Medical Department, Bristol Laboratories, 630 Fifth Ave., N. Y. 20, N. Y.

BRISTOL LABORATORIES • SYRACUSE, NEW YORK
Division of Bristol-Myers Company



ACUTE BRONCHITIS

SYNCILLIN
250 mg. t.i.d.

H.F. 45-year-old white female. First seen on Aug. 24, 1959 with acute bronchitis of 3 days' duration. Culture of the sputum revealed alpha hemolytic streptococci. A 250 mg. SYNCILLIN tablet was administered 3 times daily. Another sputum culture taken on Aug. 27 showed no growth. On Aug. 30, the patient appeared much improved and SYNCILLIN was discontinued.*
Recovery uneventful.

Illustrative case summary from the files of Bristol Laboratories' Medical Department

THE ORIGINAL phenethicillin

SYNCILLIN®

(phenoxyethyl penicillin potassium)

FIRST SYNTHESIZED AND MADE AVAILABLE BY BRISTOL LABORATORIES

A dosage form to meet the individual requirements of patients of all ages in home, office, clinic, and hospital:

Syncillin Tablets – 250 mg. (400,000 units)... Syncillin Tablets – 125 mg. (200,000 units)
Syncillin for Oral Solution – 60 ml. bottles – when reconstituted, 125 mg. (200,000 units) per 5 ml.
Syncillin Pediatric Drops – 1.5 Gm. bottles. Calibrated dropper delivers 125 mg. (200,000 units)

*Streptococcal infections should be treated for at least 10 days to prevent the development of rheumatic fever and as prophylaxis against bacterial endocarditis in susceptible patients.

Complete information on indications, dosage and precautions is included in the circular accompanying each package.

BRISTOL LABORATORIES, Div. of Bristol-Myers Co., SYRACUSE, N.Y.

BRISTOL™

Future Medical Meetings and Postgraduate Education

The Arizona Medical Association 70th Annual Meeting

April 26 through 29, 1961

Safari Hotel, Scottsdale, Arizona

FACULTY

Scientific Session, April 27-29

Herbert L. Abrams, M.D.
Associate Professor of Radiology
Stanford University School of Medicine

Evan Calkins, M.D.
Chief of the Arthritis Study Unit
Harvard Medical School

Mahlon Delp, M.D.
Chairman of Medicine
University of Kansas Medical Center

Victor A. Drill, M.D.
Director of Biological Research
G. D. Searle & Company

H. Corwin Hinshaw, M.D.
Clinical Professor of Medicine
Stanford University School of Medicine

Robert T. Manning, M.D.
Associate in Medicine
University of Kansas Medical Center

J. H. Mulholland, M.D.
Professor of Surgery
New York University School of Medicine

John W. Rebuck, M.D.
Physician in Charge
Department of Hematology
Henry Ford Hospital

REGIONAL MEETINGS WINTER AND EARLY SPRING, 1961

January 26-28, 1961
Rocky Mountain Traumatic Surgical Society
Aspen, Colorado

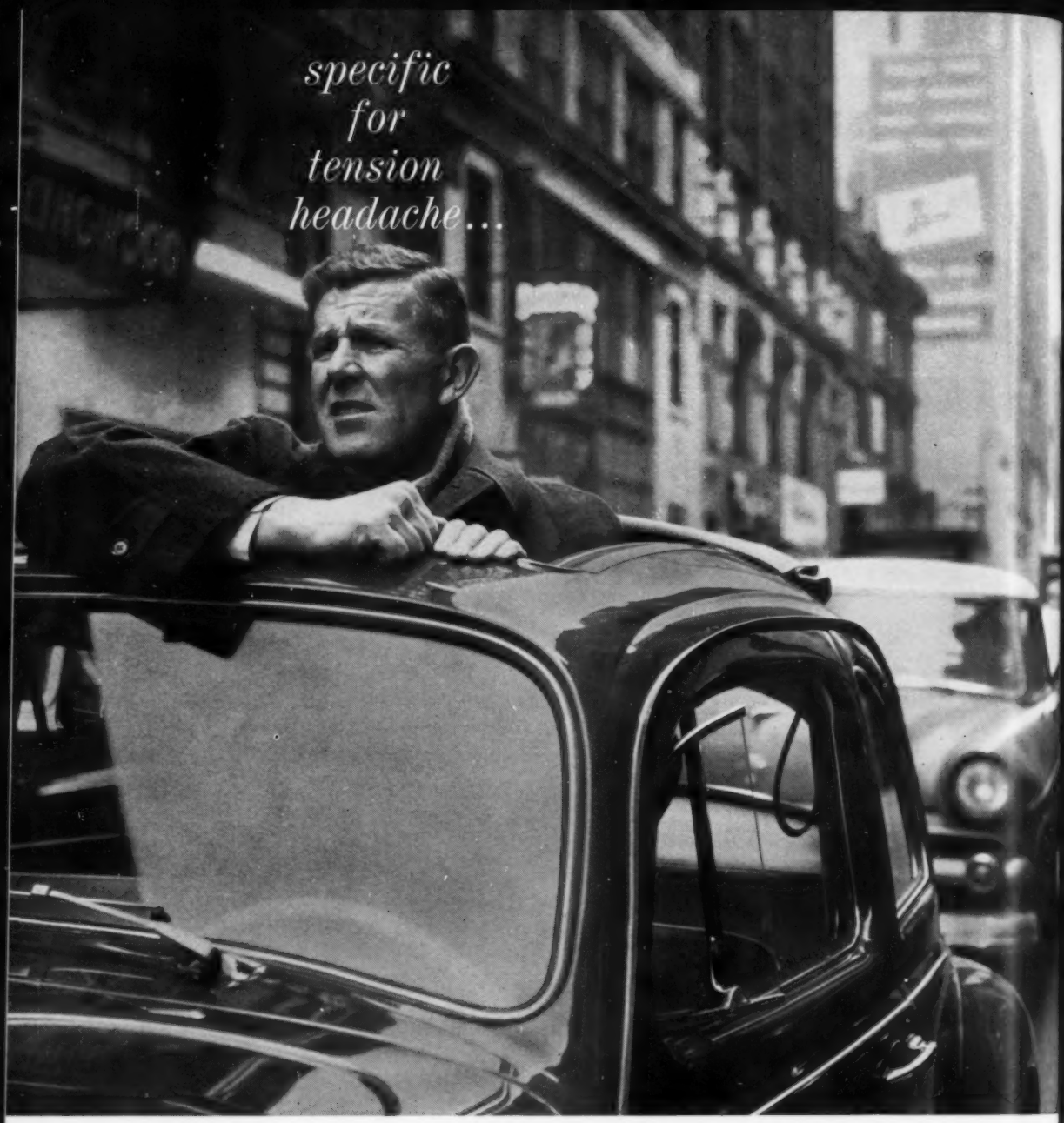
February 28-March 3, 1961
Midwinter Clinical Session
Colorado State Medical Society
Denver, Colorado

March 13-15, 1961
Gynecology
University of Utah College of Medicine
Brighton, Utah

March 20-24, 1961
Postgraduate Course – Medical Technology
University of Colorado School of Medicine
Denver, Colorado

March 28-30, 1961
Cancer Seminar, Nevada Division,
American Cancer Society
Reno, Nevada

April 17-20, 1961
General Practice Review
University of Utah College of Medicine
Salt Lake City, Utah



FIORINAL®

relieves pain,
muscle spasm,
nervous tension

rapid action • non-narcotic • economical

"We have found caffeine, used in combination with acetylsalicylic acid, acetophenetidin, and isobutylallylbarbituric acid, [Fiorinal] to be one of the most effective medicaments for the symptomatic treatment of headache due to tension."

Friedman, A. P., and Merritt, H. H.: J.A.M.A. *163*:1111 (Mar. 30) 1957.

Available: Fiorinal Tablets and New Form — Fiorinal Capsules

Each contains: Sandoptal (Allylbarbituric Acid N.F. X) 50 mg. (3/4 gr.), caffeine 40 mg. (2/3 gr.), acetylsalicylic acid 200 mg. (3 gr.), acetophenetidin 130 mg. (2 gr.).

Dosage: 1 or 2 every four hours, according to need, up to 6 per day.

SANDOZ

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